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"Drugs – Fact fallacy and Fraud"

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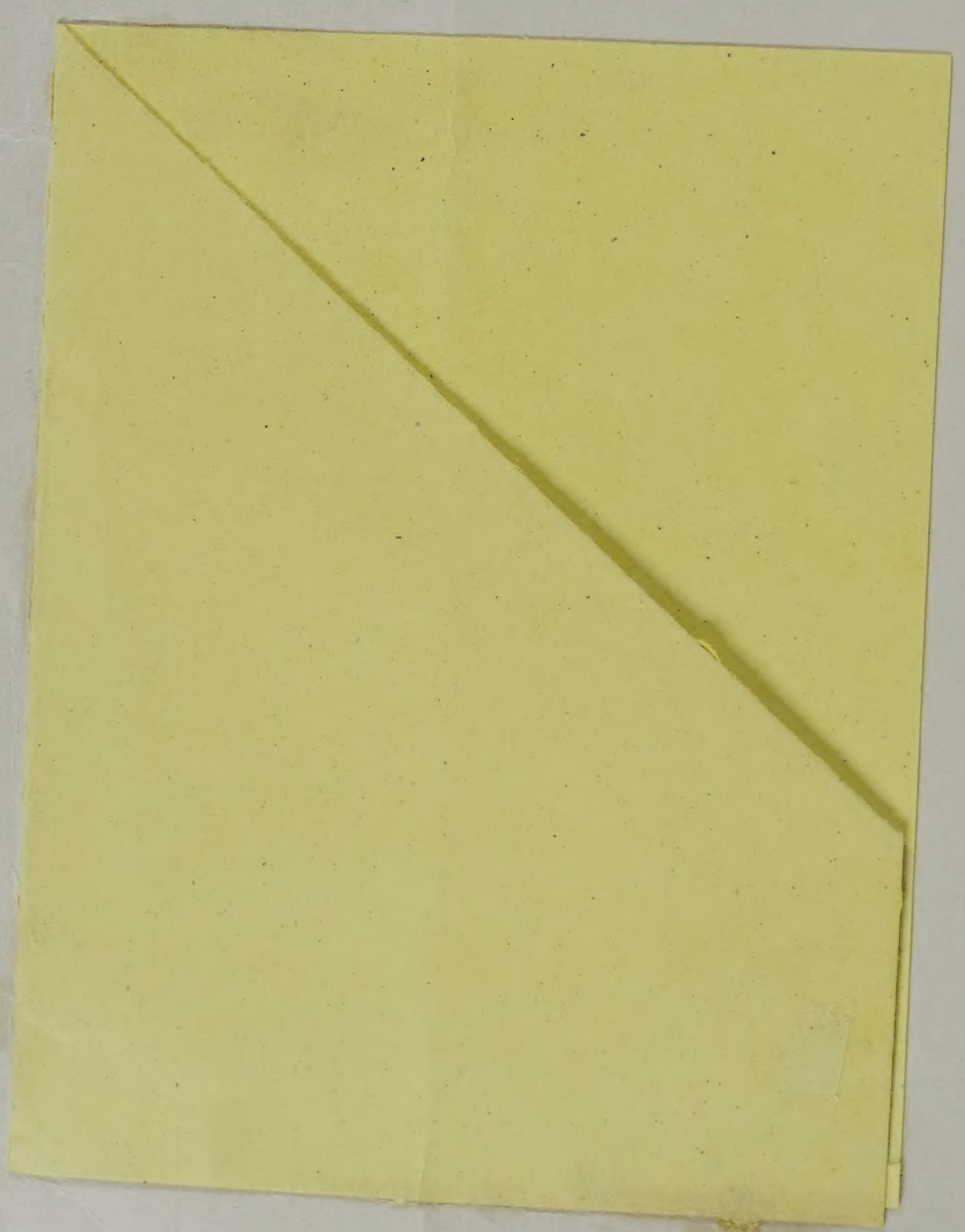

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EDITORIAL

THE DRUGS ISSUE - FACT, FALLACY AND FRAUD !!

The drug issue today, a global one, truly embodies various contradictions, disparities, exploitation, and injustice that have currently become part and parcel of all social and economic orders. This issue however has a more poignant dimension because it is intimately related to the quality of life and the right to live of a considerable segment of the world population, chiefly of the developing and the least developed countries.

This human problem requires pointed attention and concerted action, because of the mounting evidence that much of the human suffering related to drugs and the lack thereof can be alleviated effectively through rational, and just policies and practices governing the drugs trade.

Some of the crucial aspects related to this issue are the actual medical need for drugs, their availability, cost, potential for side effects, cost benefit analysis and the presentation of the product, as well as the perception of the role of drugs. A survey of the health scene in a given context is very basic to highlight these aspects so as to draw appropriate conclusions.

For India, some of the health statistics are staggering : an infant mortality rate of 140 per 1,000 live births accounting for about 30% of all deaths, while children under five are 16% of the population, they account for over 80% of all deaths in the rural areas. The mortality rate is twice as much in the rural community as compared to the urban population. The average hemoglobin level of Indian women is well below the normal requirement; half of the world's 20 million tuberculosis patients and a third of the 10 million leprosy patients are Indians. Filariasis afflicts 14 million; 48% of children below five suffer moderate to severe malnutrition; 56% of deaths in India are from preventable causes; above 80% of illness in our country can be prevented by good water supply and sanitation programmes.

Of the 9 million blind in the country, about 5 million are curable. 25,000 children go blind annually due to Vitamin-A deficiency and another 5 million suffer from related night blindness, dry eyes and rough skins. The preventable diseases which generally afflict the poor, constitute 36% of all diseases for the whole country, but account for 56.5% of all deaths.

An overview of the health scene and the existing realities in our context clearly demonstrate that the root causes of the disease and disablements widely prevalent in the country, are environmental and socio-economic : bad sanitation and unhygienic practices ; poor drinking water, inadequate and inaccessible health facilities; abject poverty and malnutrition and low levels of education and literacy. Against the back drop of these factors which conspire to produce ill-health, infections, particularly in the young, take a heavy toll.

The spending on drugs per person per year is less than one dollar in the underdeveloped countries as against more than 70 dollars per head among the developed nations.

It is thus imperative that the limited resources we have for health needs should be utilised according to priorities which can stand close scrutiny. Without waiting for the economic condition to improve the developing countries can improve their health status by rational and judicious use of the limited resources available. It is necessary to ensure that essential drugs needed for primary health care are made available to the under-served section of the rural population.

Essential drugs which can control an overwhelming majority of the problems, even in relatively sophisticated societies, number around 200 as determined by the W. H. O. For the village and the urban slum-dweller, great miracles can be achieved with fewer than 30 well chosen drugs. Elsewhere in this issue of your Journal, you will find the model list of essential drugs recommended by the W. H. O. as well as a selection of twenty of the most essential drugs, compiled by the Christian Medical Commission for use in community level health-care.

The drug industry is an avowed commercial activity and understandably, is concerned with profits and not with the health-needs of the people, eventhough their publicity campaigns would have the public believe otherwise. Hence the pace of the Essential Drugs Programme, where profitability is relatively less for the pharmacological industry, has been too slow to meet urgent health requirements.

The Director of the office of Health Economics, U. K., a drug-industry backed organisation, summed up the situation when he said "We are Businessmen, not Bishops".

The "drug mentality", the idea of a pill for all ills, remains very strong in the medical profession and is powerfully reinforced by the pharmaceutic industry. Many underdeveloped nations spend 30 to 50% of the total health budget on drugs, while the industrialised nations expend only 10%.

The major part of the drug expenditure of most under-developed nations is used to purchase therapeutic drugs rather than for prevention. What is more unfortunate is that a good part of the drugs is still imported using precious foreign exchange we can ill afford.

A study done in Africa showed that in the larger hospitals, upto 40% of drugs used were expensive proprietory preparations rather than generic alternatives. Many of these drugs were for symptomatic relief only without well-documented evidence of their efficacy. 10% of the drug budget was spent on tranquilisers, sedatives and anti-depressants of questionable indication. The proprietory drugs used, accounted for 85% of the total budget. 75% of the National budget was spent on drugs for hospitals, where only 1/3 of the medical intervention took place.

In India, the scenario is not very different. While in large urban hospitals expensive therapy of a none-too-different-level from the affluent countries, is available to the political and social elite, the 80% rural poor are devoid of even essential drugs.

Resources are finite; only a policy based on social justice is likely to improve the situation in favour of the neglected and deprived rural population.

Medical professionals are often made to believe that drug prices are closely linked to Research and Development costs. Scrutiny of this claim reveals that large foreign drug companies spend only 0.83% of the total costs on Research and Development as against 33 % for sales promotion, administration and actual expenses. In many developing/under-developed countries there is only one drug representative for every 3 to 4 doctors as against one for every 20 doctors in Britain. The budget for promoting drugs in the under-developed world remains twice as much, for most international cartels when compared to promotional expenses in the Western countries. The fact that many drugs banned in the West are promoted assiduously in the under-developed world, playing down the contra-indication, side effects and other relevant medical information is indeed a sad testimony on honourable human intentions. Dubious sample-giving practices, monetary incentives offered to key medical professionals to buttress sales, tall and misguiding claims made for drugs without adequate scientific documentation and corrupt commercial practices in the drugs-field should alert the medical profession against the onslaught of the pharmaceutical industry on the ethics of medical practice. Abolition of sampling of drugs as well as personal contacts between medical professionals and the drug-industry are likely to go a long way to mitigate the evil.

In Bangla Desh, when the Government banned a whole lot of non-essential drugs, which was indeed an expression of political will in favour of the poor, the measure drew immediate protests official and otherwise from the U. S. A. against what was construed as an "unjustifiable/ unwise measure".

There is little reason to expect that restrictive legislation in favour of the poor will not be greeted with strong protests from the powers that be. Measures to rationalise drugs expenditure in the Third-world countries are unlikely to succeed, unless such radical changes in health policies are backed up by political will.

Until then, 'Health for all', a basic human right, will remain a mirage.

S. J.

JESUS' MINISTRY OF HEALING

Fr. Francis Martin

CORNELIUS, the centurion, had assembled his household to hear Peter tell them the Good News. Peter told them about Jesus' ministry among them, and when he spoke of the resurrection and the forgiveness of sins, "the Holy Spirit came on all who heared the message". (Acts 10, 44). In this context, it is interesting to note Peter's words summing up Jesus' activity.

You know what has happened throughout Judea, beginning in Galilee, after the baptism that John preached - how God anointed Jesus of Nazareth with the Holy Spirit and power, and how he went around doing good and healing all who where under the power of the devil, because God was with him. (Acts 10, 37-38).

We wish in this article to reflect on that aspect of Jesus' activitiy by which, through healing and other miraculous deeds, he announced and made present the Kingdom of God.

The fact of Jesus' miracles

Once, as Jesus stood in Capernaum, he looked up to the town on the hill at the back of the city, to Korazin; then his gaze went out over the water of the sea of Galilee to another town a few miles north, to Bethsaida. He thought of all that he had done in these three places to proclaim the Kingdom of his Father and how hardened the hearts of his countrymen had become in the face of all this. He grieved over their loss and he was angry over the affornt they offered to the immence mercy of the Father. In prophetic words he announced their future. No one who has stood on the ruins of Capernaum looking up the hill to the spot where the overgrown ruins of Korazin now stand and then over to the ruins of Bethsaida, can help but be chastened by the thought, of what it means to ignore God's offer of salvation and the signs he works to bring us to turn from our sins.

Then Jesus began to denounce the cities in which most of his works of power had been performed, because they did not repent; "Woe to you, Korazin! Woe to you Bethsaida! If the works of power that were performed in you had been performed in Tyre and Sidon, they would have repented long ago in sackcloth and ashes. But I tell you, it will be more bearable for Tyre and Sidon on the day of judgement than for you. And, you Capernaum, will you be lifted up to the skies? No, you will go down to the depths. If the works of power that were performed in you had been performed in Sodom, it would have remained to this day. But I tell you that it will be more bearable for Sodom on the day of judgement than for you." (Mt. 11, 20-24).

It is worth observing that this saying of Jesus is the only evidence we have of his activity in Korazin. If a gospel writer had framed a statement of Jesus in order to convey his message of repentance, he would have mentioned some other towns, Nain, Magdala, Caesarea Philippi, which were at least named in the tradition. We have here a prophetic statement of Jesus himself in which he appeals to his "works of power" as a motive for repenting and believing the Good News.

The aspect of Jesus' activity was so well known that when later Jewish tradition tried to explain why Jesus was crucified, they never thought of denying the Christian claim to Jesus' miraculous curse and exorcisms, rather they attributed them to magic. We find the beginnings of this controversy already in the gospels, when the pharisees, so hardened by their resistance to Jesus that they are able to call good evil, attribute his exorcism to "Beelzebub" (Lord of the Flies)-a popular name for satan. Jesus' answers, perhaps delivered in several different occasions, are summed up for us in the gospel tradition. There are three answers : first, an argument from common sense; second, an argument drawn from the power God had given to other men in the Jewish world to drive out demons; and third, an argument based on the fact that Jesus, who expels demons in the force of his own authority, is the Stronger One already mentioned in Is. 49, 24–25. This is the text of Jesus' answers.

FIRST Every kingdom divided against itself will be ruined, and every city or household divided against itself will not stand. If satan drives out satan, he is divided against himself. How then can his kingdom stand?

SECOND And if I drive out demons by Beelzebub, by whom do your people drive them out? So then they are your judges. But if I drive out demons by the Sprit God, then the Kingdom of God has come upon you.

THIRD Or again, how can anyone enter a strong man's house and carry off his possessions unless he first ties up the strong man? Then he can rob his house. (Matt. 12, 25-29).

Why did Jesus work miracles?

"If I drive out demons by the Sprit of God, then the Kingdom of God has come upon you." Jesus does not only speak about the Kingdom of God, he brings it about. When John the Baptist sent messengers to Jesus asking if he were the "One to Come," Jesus answered by pointing to the fact that the prophecies of restoration and redemption found especially in various chapters of Isaiah were being fulfilled.

Then will the eyes of the blind be opened and the ears of the deaf unstopped. Then will the lame leap like a deer, and the tongue of the dumb shout for the joy.' (Is. 35, 5–6).

The spirit of the Lord, Yhwh, is on me, because Yhwh has anointed me to preach good news to the poor. (Is 61, 1)

Go back and report to John what you hear and see: The blind receive sight, the lame walk, those who have leprosy are cured, the deaf hear, the dead are raised, and the good news is preached to poor. (Mt. 11, 4 & 5).

God has promised us eternal life, a life with him forever. Salvation is the gift of this life in all its fulness. As St. Paul puts it we are experiencing the first-fruits of this life and we await its perfect realization: "Not only so, but we ourselves, who have the first fruits of the Spirit, groan inwardly as we wait eagerly for our adoptions as sons, the redemption of our bodies," (Rom 8, 23). When Jesus healed people he was proclaiming the fulness of salvation that God the father was making available to us in his Son. Healing is God's "audio–visual aid" so to speak. Jesus proclaimed the Kingdom and the life with God to which we are called, but he also illustrated the meaning of the new life by healing the sickness of the body as well as those of the soul. In this way people would understand what new life really means and wouid have confidence in the power of God to change their lives.

As people heard Jesus preach, hope came into their lives. They began to understand that, if they would turn from their sin, God would forgive them and give them a new relationship with him. They reached out in trust to receive forgiveness and new life, and they accepted Jesus as the one sent by God to bring his message. This is what the synoptic gospels mean by "faith". Notice how this process is described in the story of the woman who was healed of a haemorrhage.

Just then a woman who had been subject to bleeding for twelve years came up behind him and touched the edge of his cloak. She said to herself, " If I only touched his cloak, I will be healed " Jesus turned and saw her, "Take heart daughter," he said, "your faith has healed you." And the woman was healed from that moment. (Mt. 9, 20–22)

The woman knew that contact with Jesus would be enough to heal her-the word for "healing" and "salvation" are the same in greek-and she reached out to touch him, Jesus acknowleged her faith and said that it has brought her wholeness (healing/salvation). For those who came to know of it (and this includes ourselves), this healing was a lesson in the extent of Jesus' compassion and power, and a symbol, an "audio-visual aid" showing us how to receive salvation: we must reach out and touch Jesus. Of all those who bumped against Jesus as he walked along the way, only one "touched" him. That manner of touching is still availabe to us—it is faith.

When Jesus annouced the coming of the Kingdom of God, His words were not merely the description of some ideal for which men should strive, they brought

about the reality they proclaimed. His words were an invitation to enter into something that existed. Those who accepted this invitation experienced in their lives, often in their bodies as well, the truth of what Jesus proclaimed. Where did this power come from? Mathew is careful to point to the sourse of all this saving power; it is the death and resurrection of Jesus. The healings that Jesus worked were a sign as well as an anticipation of the power that would be available to mankind through the Cross. Notice how Mathew concludes his account of Jesus' first day of ministry at Capernaum with a quote from the fourth "Servant song".

When evening came, many who where demon-possessed were brought to him, and he drove out the spirits with a word and healed all the sick. This was to fulfill what was spoken through the prophet Isaiah ; "He took up our infirmities and carried our diseases" (Is. 53, 4). (Mt. 8, 16-17).

When Jesus healed them, or when he heals now through the prayers and the ministry of those who believe in him, the ultimate reason is the same. It is to bring people into contact with the Life-giving power of his death and resurrection so that they will know for themselves who he really is and what is the new life of the Kingdom he has come to inaugurate. When we read the stories in the gospels. we are given the eyes with which we can behold the works of the Lord in our midst. We know how to understand the healings, the changed lives, the new found joy and meaning to life that those who give their lives to Jesus come to experience.

The one sign that is always present to bring to us the knowledge of Jesus is the sign of the Cross; it is a sign of Life. In John's gospel we see this other side of the role of faith in regard to the healing and saving work of Jesus. Signs lead to belief in that they are meant to bring us to a living personal knowledge of Jesus.

Do you not believe that I am in the Father and the Father is in me ? The words that I speak to you I do not declare on my own. The Father abiding in me is doing his work. Believe me : I am in the Father and the Father is in me. Or else, believe because of the works. (Jn. 14, 10-11).

"Believe because of the works". The Lord is telling you : Believe because of what the gospels tell you of me, of the words I spoke and works I performed, If you read and beg the Holy Spirit to enlighten you, you will come to understand and reach out and be saved. Continue to believe. Look at the wonders I am doing in your own life. Believe because of the works; reflect on what Ihave done for you, ponder it. Soon you will come to see that all power for good in your life, all the resources available to you enabling you to die to sin and lead a new life, come from my Cross. If you will hold fast to this under standing and let my Power change you, you will come to know who I really am. My Spirit will reveal to you the transcendent and glorious position that I hold at the right hand of the Father You will know that I am the son of God. Then the work of salvation will become mature in your life and, as I told my first disciples. so I tell you: he who believes in me will do the works that I do, and even greater things than these, because I go to the father."

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ROLE OF DRUG INDUSTRY—IN PERSPECTIVE

In 1978, the world market in pharmaceuticals was estimated to be 70,000 million US dollars Of this 85% of the market was to be found in the industrialised nations (65 % in countries with a mixed economy eg. Western Europe, North America, Japan etc. and 20% in the socialist countries in Europe).

The pharmaceutical market in the developing countries amounted to 15% of the total (6 % in Latin America, 7 % in Asia and 2 % in Africa).

Of all pharmaceuticals produced, 85 % is produced by the industrialised nations and only 12 % by the developing countries. That results in a commercial deficit for the developing nations (which consume 15 % of the global production) to the tune of 2,000 million US dollars.

The expeniture on pharmaceutical products by any community presently depends on the purchasing power of the consumers than on the real health needs of the population. In Middle East many drugs cost 3 times or more for the same product compared with prices in India.

Perhaps the first point to remind ourselves is that the drug industry is in fact a "commercial enterprise where profit making is the ultimate motive and when we castigate the drug industry for making enormous profit, we are perhaps overemphasising on what should be obvious. So long as there are no firm/absolute statutes to govern, manufacturing, marketing and pricing policy of drug firms, it would be only natural that demand and supply equation would be the only rationale governing practice.

It is somewhat of an anomaly that in the making of health the commercial organisation of pharmaceutical industry is married to the "service organisation" of the medical care facility. So it is perhaps understandable that the pharmaceutical industry seeks to project the image before its partner in arms of being a dutiful service organisation. The medical partner is often rather obliging and strives to preserve the image of a happy marriage. In this alliance though one may like to believe that both partners are equal the fact remains that this is not so and hence the stronger partner, the pharmaceutical industry dominates the alliance. The struggle for emancipation from this relationship may well sound like pages from the 'womens' lib' movement.

Suffice it to say that the pharmaceutical industry is rich, powerful, influential omnipotent with right contacts in the right places and offers right incentives, and is a 'smooth operator' often operating under deceptively benevolent guises. They have their tentacles reaching out all over the globe to people who matter commercially, exhibiting all the trappings of an 'undercover agent' who is destined to become a legend.

These facts and more ought to convince all that none can wish them away. It would also be not just to say that the pharmaceutical industry does not make contributions to development of medical science. "International companies like Ciba, Burroughs Wellcome and some others do spend significant amount of money on research and on supplying the medical profession useful information, however small this expenditure may be in terms of their gross turn-over or profit.

Even though malpractices abound in this field of pharmaceutical industry, just denigrating them with hyperbole will not serve real purpose. It has become fashionable to bathe in the sunshine of puritanical glory that comes from the ritual of dressing down and devouring pharmaceutical and other related health industry as vested interest monsters devouring the health of the people.

I hold no brief for the pharmaceutical industry, but it is my purpose to draw our attention to the fact that the problem we are faced with of the health robbery is a highly complex one where there is

collusion between various vested interested groups among which the pharmaceutical industry is a well defined and powerful agent. Perhaps it is easier to deal with avert partners in this game such as the pharmaceutical industry, than the various covert forces in the society, which are colluding with vested interest forces, but in public gaze ostensibly striving to uplift the masses and to further the interests of the under-privileged group.

The pharmaceutical industry as a commercial organisation is well within its defined goals to promote their own commercial interests among the consumers of their products either directly or through the intermediary organisation of the medical profession. The concept of 'medical ethics' is an old fashioned idea which appears to have lost its credibility and value. The American Medical Association and like minded peer groups take an increasingly lenient view of what 'medical ethics' connotes. This change in perception they would have us believe, is in the interests of the public to enable them to get the best value for money spent. Meantime the pharmaceutical and other related health care industry are having a field day. The learned judges of our Supreme Court have ruled that hospital is an 'industry'. It is indeed a paradox that to make any product, even a tape measure, several ISI standards have to be satisfied, but 'health care industry' has no standards to be met regarding its product, no holds are barred and understandably we have a 'free for all' situation on hand.

The pharmaceutical industry offers incentives and attractions to all its customers who include the retail pharmacies, the medical professionals and the consuming public. It assures the public of a happy, healthy and long life through promotion of their health utilising the health making products marketed by them. To the professionals, decision makers regarding drug purchase and the retailers they offer happy and sumptuous lives by promoting their wealth. So the logic would appear that if health is wealth, for the public, wealth is health for those who promote their commercial interests.

The pharmaceutical industry concentrates on promoting their drugs in the first place in the medical college hospitals, often offering large bonuses to these institutions. This is done not with view of immediate returns in terms of sales, but out of a carefully calculated long term goal of promoting their brand products among the medical students. The industry has closely monitored, researched and learned that most doctors continue to have first preference and prescribe mostly drugs/brand names they first learned while in the medical school. So this seed sown in the medical school is carefully nurtured with follow up incentives in the form of medical samples, gifts, curios etc. Depending on the doctors obliging nature and his power to pay the industry back in kind, proportionate economic incentives are offered. As a doctor in practice for the past 24 years I am often appalled at the nonchalance with which commercial deals and offers are made by the pharmaceutical industry, as years go by. This must surely mean that we now have a situation where the pharmaceutical industry makes little apology for making commercial overtures to medical professionals, who according to time honoured standards/expectations are the custodians of public interest

Pharmaceutical industary under-writes the expenses of medical conferences, many of which are held in 3 or 5 star hotels again depending on the 'clout' the organised professional group holds to further the industries' vested interest. I have learnt that a baby food company met all the expenses of the entire group of delegates from their country attending an international paediatric conference!. International conferences themselves are a big scandal and it is little wonder that the organisers fight between them after conference, for appropriating the spoils. So to make a catalogue of malpractices indulged in by vested interest group health care industries would run into several pages and

touch many a gentlemen from whose cupboard many a skeleton is likely to be unearthed.

For an exhaustive and well researched account of the role of pharmaceutical industry in exploiting the health scene, the April-June '81 issue of Health for the Millions, offers the best reading and it can bear repetition.

In 1976 Rs. 700 crores worth of drugs were produced in India. Of this 25 % was spent on vitamins, tonics, enzymes etc., 20 % on antibiotics and only 1.4 % on anti-Tbc. drugs. We are not self-sufficient for our requirement on antileprosy or malaria drugs. More chloroquine is imported than produced locally. Primaquin and Trimethorpim are not locally produced. Vaccines against influenza, measeles, mumps and polio are all imported. Out of 81 major drugs sold against infections, parasitic diseases, respiratory ailments and C.N.S.diseases, 28 are imported. There is stiff resistance from the pharmaceutical industry and doctors against use of generic names in favour of brand names.

80-90 % of drugs produced by some major foreign owned drug companies consists of simple household remedies, life saving drugs account for less than 1/3 of the total value of goods, sold by these firms.

The production for essential drugs is less than the installed capacity, as low as 50% in some cases, whereas the production for vitamins, tonics and general items, often far exceeds the licenced capacity.

Facing brass tacks

In 1979 WHO determined, after careful study that a range of just over 200 active substances can just about cover the health needs of the majority of the population. A supplementary list of about 45 drugs could serve as optional ones to be used in the event of resistance to the use of essential drugs, in rare disorders or exceptional circumstances. (WHO technical report series No. 641) : By the end of 1981 another revision is due of this list.

In India, Hathi committee as recommended just 116 generic names. Ramalingaswami committee (1980) has prepared a list of essential drugs at the community level against the back drop of the national alternative strategy for Health for all by the turn of the century. This includes about 18 items only (Refer : Health for the Millions April–June 1981).

In our country, as we have seen, the home work is complete and action blue prints are ready for a true revolution in health care and to mitigate the injustices now prevalent in health care. The lament unfortunately, is that the political will to implement such revolutionary changes is conspicuous by its absense. This is where the impasse is for us. The road ahead is frought with uncertainties and the credibility gap between drawing action plans and implementing them is fast approching cent percent.

The goals that one should set probably need be realistic, modest and achievable. In the first place a national health policy should be made enlisting the support of all political parties, the executives, health professionals and the public and involving the related health care industries as well, to the maximum extent possible. The policy should be functional and the political will to implement the same should be genuine and forthright. Such a policy should touch upon all aspects of health care where presently injustices, inequity and exploitation are prevalent. A policy of this kind should Include, the following features.

1) Drugs should be considered as essential elements in health care related to basic human rights of an individual and not as a consumer product. Pattern, availability and cost should reflect the real priorities and needs of the people.

2) List of essential drugs should be drawn with the help and advice of the medical professional group in tune with the WHO recommendations. These products should be further delineated and streamlined for different levels of the health system.

3) Responsibility for manufacture of essential drugs should be taken up by the Government. Strict quality control

measures should be adopted to ensure good quality of essential drugs. The technical co-operation offered by WHO in this area should be fully utilised. Bulk drugs may be imported again under the technical co-operation of international organisations like WHO, perhaps co-ordinated on a regional geographical basis to get the best advantage of competitive bidding. WHO and the World Bank or in some cases the regional development banks have already collaborated in a number of such projects, in some parts of the world. Technical co-operation between developing countries, one of the priorities within the United Nations system, should be fully harnessed to mutual benefit.

4) Supply of essential drugs should match national requirements fully and an effective distribution system should be operative to ensure availability of these drugs at the most peripheral level.

5) The national health policy should be fully endorsed and made applicable to all the states in India.

6) Private drug companies should not be allowed to market essential drugs or formulations incorporating these.

7) All ethical drugs should be marketed by pharmaceutical companies under generic name only.

8) Drugs patent system should be reviewed and linked to actual expenses in devoloping new drugs.

9) All sampling of drugs and offering of incentives and complements to doctors, hospitals and other related personnel should be banned.

10) Promotion of ethical drugs should be made only or mostly through mail information service Direct contact between medical representatives and health professionals should be discouraged.

11) No advertising in public news media by drug firms should be allowed directly addressed to the public or ostensibly to the medical proffessionals. Drug advertising should be banned on cinema, television and other public media. Tobacco, liquor and pharmaceutical industry should not be allowed to promote their vested interests subtly behind the smoke-screen of promoting games, sports and such public events.

12) Medical organisations should be prevented from accepting sponsoring of their professional activities by drug firms. Medical professional groups should be encouraged to practice prudence, moderation and austerity in their group activities without dependance on drug or other health care industry.

13) The health personnel should be adequately trained at all levels with the technical cooperation of WHO and other related international agencies in identifying correct global and national health priorities and deploying the right techniques and approches to treatment including full knowledge on relevance and application of essential drugs. Medical professionals should be imparted through knowledge and made conscious of costs and the national constraints. A sense of belonging to a team of workers engaged in a National crusade should be carefully cultivated. Presently health care professionals have hardly any social or National perspective; even teachers are ignorant of these.

14) Medical curriculum should be restructured to incorporate National priorities to draw sharp focus beyond individual health to social health care, National and inter-national health policies and priorities.

15) Countinuing education should be made mandatory for all health professionals especially the specialists, so that they may keep themselves abreast of changing trends and techniques in medical care.

16) WHO and related internationally accepted health organisations should lend their credentials to the "Essential drugs industry", so that the pharmaceutical industries ploy of decrying drugs produced locally as "poor quality", can be effectively countered.

17) Voluntary organisations should lend their full support to National health policy and streamline their activities in conformity with the national priorities. They should also supply effective feed back on the implementation of National policies.

Dissemination of information to the public and the health care professionals about malpractices and dubious priorities on the part of the pharmaceutical industry should be facilitated.

18) A consumer movement after the style of " India Health Vigil action network " may be organised to monitor practices regarding health care by the industries involved and to seek suitable redress of grievances through democratic means.

19) Pharmaceutical firms should be pressured to bring out package inserts which are truthful incorporating the ill-effects of the drug in full and the possible limitations.

20) Drugs banned in the developed countries (for whatever reason) should not be marketed in India. There is no substantive evidence that the pharmacodynamics or toxicology of drugs is significantly different between the 'West and the East'.

International Federation of Pharmaceutical Manufacturers' Association (IFPMA)

The code of pharmaceutical marketing practices proposed by the IFPMA should be properly studied at the national level.

The proposed code would appear to be a clever attempt at pre-empting international action such a WHO sponsored international code of conduct of marketing practices of Baby Foods. The proposed code seeks to maintain the rights of the industry to practice dubious methods. As a code it has 'no teeth' to monitor or act in the case of dubious practices and no punitive action is suggested. It maintains the right to have medical representatives to promote commercial interests of the industry with doctors. The right to 'sampling' is maintained under the guise of familiarising the profession with their products. Hosting symposia, congresses and other means of verbal communication is stoutly defended and only embellished by the new found principal focus on 'scientific objectives'. The major malpractice modalities are however well preserved.

This document is worded so sutly that on cursory examination it would appear to offer major concessions on the part of the drug industry and accept self-imposed restrictive practices.

Organisations like WHO/UNCIAD could use this proposal as a talking point with the industry, but international professional and public opinion should be mobilised to achieve a code of practices which would be deep, effective and meaningful.

In 18th century France, Voltaire lamented that " physicians prescribe medicine of which they know little to cure diseases of which they know less in human beings of which they know nothing ". If Voltaire were alive today he would probably add to benefit the drug industry which they know intimately ".

In conclusion we may say that the onus lies on each one of us to emancipate the people from the " Great Health Robbery " underway. It would perhaps be fitting to wind up with the Biblical admonition " cast out first the beam out of thine own eye ; and then shalt thou see clearly to cast out the mote out of thy brother's eye."

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ESSENTIAL DRUGS FOR THE THIRD WORLD

Vittorio Fattorusso

Rather than wasting money on pharmaceuticals they do not need, developing countries should make judicious choice, and wise use, of items figuring on the model list recommended by WHO of some 200 of the essential drugs which can cover the needs of the majority of the population.

The world market in pharmaceutical products was estimated in the year 1978 to amount to US $70,000 million. Of this market, 85 per cent is to be found in the industrialized world, including about 65 per cent in countries with a mixed economy (Western Europe, North America, Japan and so forth) and 20 per cent in the socialist countries of Europe.

The pharmaceutical market in the developing countries, where the majority of the world's population live, only represents 15 per cent of the total, including about 6 per cent in Latin America, 7 per cent in Asia and 2 per cent in Africa.

As for actual pharmaceutical production, it was estimated that 88 per cent of it stems from the industrialized world countries, and only 12 per cent from the developing countries. Since the latter consume 15 per cent of the world production, they obviously had a commercial deficit in 1978 amounting to three per cent, that is, about $2,000 million.

This gap between developing and industrialized countries persists. The figures above are not intended to be very precise, but they do clearly show that, from an economic point of view, the consumption of pharmaceutical products follows tendencies which are not very different from those of other manufactured goods; the amount spent on pharmaceuticals depends rather on the purchasing power of consumers than on the real health needs of the population.

This in turn explains why spending on drugs per person per year comes to less than one dollar in the least developed countries, yet can exceed $70 in certain industrialized nations.

Again as regards spending on pharmaceuticals, there can be considerable differences between one developing country and another, whether in the proportion of expenditure in towns as compared to rural areas, or in the wise or unwise use that is made of resources—for instance in selecting what type of medicaments should be available, or in deciding the use to be made of them in health care.

Without needing to wait for their purchasing power to increase, the developing countries can improve their situation simply by rational use of the limited resources that they have available for buying drugs. The judicious choice and wise use of medicaments can help to cut down on waste, especially in the urban areas, and can ensure that the essential drugs needed for primary health care are made available to under–served sections of the rural population.

The increase in prices of medicaments on the world market is of concern to all countries, but especially to the developing ones where the resources aviailable are very limited. The unit prices certainly important, but other factors have to be considered, such as the effectiveness of the drug, the method and frequency of administering it and the costs involved, its stability in tropical climates, and so on. So we have to take into account the total cost and the efficacy of all the prophylactic and therapeutic measures that are possible under local conditions.

In most developing countries, health care is limited to urban areas where there are doctors, pharmacists and hospitals, while the majority of people living in

suburban and rural areas remain more or less neglected. Drawing up a more equitable health policy, based on the development of primary health care, calls for a firm policy on essential drugs, based on the real needs of the majority of the people of these countries.

Under such a policy, the selection of essential drugs for the different levels of the health system in crucial. When we observe the proliferation of pharmaceutical products whose efficacity and safety have not yet been proved, or whose indications have nothing to do with the real needs of most people in the Third World, we have to make a rational choice if we are to make the best possible use of available resources.

So why don't these countries follow the good example set by the most advanced hospitals, whose list of drugs they keep available are not very different-apart from those needed for control of tropical diseases-from the list of some 200 items drawn up by the WHO Expert Committee on the Selection of Essential Drugs? would the result be, as certain critics have claimed, to lower the quality of health care in these countries? I don't think so. Experience shows that this kind of rationalization can help to avoid wasting funds through buying drugs which are ineffective or unusable under local conditions, or through buying similar drugs under different brand names. Furthermore, it helps to simplify quality control, maintenance of stocks and distribution, as well as encouraging the sensible use of drugs.

Although the selection of a limited list of essential drugs which correspond to health needs, and to the standard of training of health personnel at different levels, is crucial, this measure alone is not sufficient. Even when a careful choice is made of the drugs that are most useful and best adapted to local needs, the waste of resources can continue if the health personnel don't know how to use them correctly. Thus an antibiotic which is vital in the struggle against a certain communicable disease, and under certain conditions can even save life, may also be used wrongly and with adverse effect if the indications are misunderstood or if the doses are insufficient. It thus becomes another source of waste and may even endanger the patient. Vitamin B 12, an essential drug in certain cases of anaemias, is widely used as a "tonic" although its effectiveness as such has not been proved. One can go on citing such examples indefinitely and they show the importance, even from the purely economic standpoint, of making the best possible use of drugs by training and informing health personnel at all levels.

What is more, even when a wise choice of essential drugs is made, difficulties may arise in ensuring that they are of good quality. If laboratory analysis is not available to check on them, and especially when there is a need to economise, a number of potential risks arise; whether one pays heavily or cheaply, there is a danger of wasting money on poor quality goods which will not have the expected prophylactic and therapeutic effects and may even prove dangerous.

It is certainly not a question of having products of a superior quality, with no bearing on the real needs of the patient, but marketed with glossy advertising and sold at a fancy price! What matters rather is to be absolutely sure that the product conforms to international standards: this assurance can be obtained by demanding a certificate from the health authorities of the exporting countries who participate in WHO's Certification Scheme. Where there is any doubt, the same authorities can also be asked to furnish all necessary information on the control measures they apply to the exported product.

Small developing countries simply do not have the resources needed to set up a national laboratory for drug quality control, but they can pool together to create a laboratory at the service of several countries: this fits in well with the principle of technical cooperation among developing countries, and WHO is very much in favour of such an approach.

As for countries which are planning to start their own local production of drugs, we recommend that they start with a national laboratory for quality control.

Without such a laboratory, they run the risk of not being able to check on the standards of local products, and this could prove harmful both as regards the use of these products in the country and as regards exports Obviously, it is much easier to set up a laboratory for a limited number of essential drugs than one which has to check on thousands of different brands.

As regards supply of essential drugs, the situation is critical for small developing countries, especially those which are landlocked or which are small islands. On the world pharmaceutical market, such places have little interest and they are so distant from the production centres that the manufacturers often don't even bother to respond their requests for tenders. As a result, they turn to the middle-men, who not only make them pay a steep price but once again fail to give them any guarantee of quality. Sometimes they don't even know where the products they are buying are manufactured! The solution for such countries is to pool their orders togther, as a number of islands in the Pacific are now doing. Since their bulk purchases are so much bigger, they can obtain a more reasonable price and can turn to those manufacturers who are known for the quality of their goods. WHO is already collaborating in this form of technical and economic cooperation among developing countries.

Another way of bringing down the price of drugs is to set up plants which will produce essential drugs by processing imported raw materials. In that case the authorities must be on their guard to ensure that the quality of the local production is up to international standards, and at the same time that the price of the raw materials is not excessive, otherwise local production risks becoming dearer than the imported goods. This has indeed happened in the past. WHO and the World Bank, or in some cases the regional development banks, are already collaborating in a number of projects. If a group of countries could get together and agree to have a single communal production unit, this too would count as technical co-operation between developing countries, one of the priorities within the United Nations system.

Finally, when we look at essential drugs in the context of primary health care, the problem arises of assuring distribution to the most remote areas; this implies a certain mobility of staff and materials between the centre and the periphery. It has often been said that without an infrastructure, it is impossible to distribute drugs. So the vicious circle tends to perpetuate itself : the distribution mechanism is not developed because there are no drugs to distribute, and no attempt is made to build up stocks of the priority drugs needed for primary health care. Fortunately, in a number of countries, efforts are under way to break this vicious circle and some successes have been recorded. WHO and other international organisations are to play their role in this domain at the request of governments.

The Member States of WHO have agreed on their common objective: Health for all by the year 2000. In the global strategies worked out to attain this goal, essential drugs have not been forgotten, since without these drugs the effectiveness of primary health care would be seriously compromised. In the case of communicable diseases, for instance, which are to blame for so much morbidity and mortality in the developing countries, essential drugs-including vaccines-are indispensable elements, together with cleaning up the environment and propagating health education, in improving the health of the people.

To sum up, the developing countries can, even with the limited means at their disposal, considerably improve their situation by drawing up a health policy that is adapted specifically to solving their foremost problems. The international organisations such as WHO are ready to collaborate with them in putting programmes into action which will bring the essential drugs that they need within everyone's reach. But it is up to the governments themselves to accord the necessary priority to primary health care and essential drugs.

This policy sometimes runs into certain obstacles. Some authorities consider drugs simply as consumer products which are subject to the laws of supply and demand. Others–including WHO– see them as essential elements in health care, whose availability must respond to real needs. Pressure groups have arisen–particularly among certain pharmaceutical industries and in sections of the medical profession—which would prefer to see the status quo maintained.

The international community, however, has expressed itself with absolute clarity, through the World Health Assembly, in recommending Member States to adopt a drug policy that is tailored to their health needs, and in appealing to their sense of community to help make WHO's action programme on essential drugs effective.

—Courtesy: World Health – May 1981
(The Magazine of the World Health Organization)

The Editorial board of JCMAI has resolved to bring out a new feature on *Institutional News* subject to the following conditions.

Hospitals to be asked to contribute Rs. 100 for this service which will include the following:

(a) Occupy one page of the Journal

(b) One photograph may be included

(c) Limited number of re-prints may be provided free of cost. Further re-prints will be made available at extra cost, upto two institutions may be so published in any issue of the Journal.

Drugging the Indian

In countless Third World countries, the multi-billion dollar pharmaceutical industry has long practised a particularly pernicious form of what Dr Halfdan Mahler, Director General of the World Health Organisation, once called 'drug colonialism'. In its most brazen form, this consists of 'dumping' highly toxic drugs banned in the US and Europe on unsuspecting countries like Brazil and Argentina, which have no drug regulations worth the name.

While, thankfully, the situation is not so bad here, we in India could well be victims of a more subtle drugs swindle. After all, millions of Indians still guzzle an endless array of concoctions that are either useless and expensive (vitamins, tonics, health drinks, cold 'remedies') or contain ingredients that have been withdrawn in many Western countries because of their adverse effects (phenancetin, estrogen - progesterone 'Pregnancy test' combinations) or are very restrictively sold and used abroad (chloramphenicol, analgin).

Last year, Indians bought Rs. 900 crores worth of drugs, nearly a third of them being over-the-counter (OTC) products. Today, as never before, infective diseases are our public health enemy No. 1. Yet, tonics, vitamins, 'health restoratives' and 'enzyme digestants' are brought more than antibiotics : while antibiotics constitute just 20 per cent of the entire pharmaceutical market in India, these OTC products accounts for a much bigger chunk - nearly 30 per cent of the market.

For instance, there are 10 million TB patients in India. TB claims about 500,000 lives every year, and no other disease has more victims in any other country in the world. Yet, anti TB drugs make up a paltry 1.4 per cent of the Indian drug market.

According to experts like Dr B B Gaitonde, former head of Bombay's Haffkine Institute and now a WHO consultant, there is only one reason for this tragic state of affairs : Pharmaceutical companies vying with each other to create a need for over-whelmingly irrational products rather than manufacturing drugs that meet real social needs. "It is high time" he points out, "that a technical group is appointed by the government to monitor and regulate the pattern and spectrum of drugs manufacture, so that formulation manufacturers are made to meet social needs rather than such artificially created market needs because of their predominantly money spinning value. Such a committee should apply its mind to study formulations using excessive vitamins which is a national waste, as well as irrational combinations having long-term harmful effects, and make recommendations as to the therapeutic rationale and efficacy of drugs as has been done by the US government."

In the absence of such regulations, the number of formulations marketed in this country has shot up to cover 15,000. Some time ago, the WHO had concluded that developing countries

like India really needed just about 200 essential drug formulations. Experts involved in devising the Hathi Committee report, in fact, scaled this number down to about 44. But formulations continu to proliferate, and to be sold, mainly because they are backed by sustained hard-sell campaigns.

Playing a pivotal role in such campaings are the 'detail men' or medical representatives of pharmaceutical firms. As far back as 1902, Sir William Osler, a hallowed aame in the annn!s of modern medicine, decried the 'drummer of the drug house' calling him 'a dangerous enemy to the mental virility of the general practitioner.'

One of the most potent weapons in the arsenal of the drug drummer is the free sample. Says Dr N H Antia, who heads Bombay's Foundation for Research in Community Health, "This is a very subtle but dangerous tool employed by pharmaceutical companies to push their products. Many unscrupulous doctors break open the packets or cartons, discard the tell-tale 'physicians sample' label and sell them to their patients. However, there are many others who accept these samples and give them free to their patients. Soon the patients are 'hooked' on the product, and then there are no longer any free samples ! I have seen a number of highly expensive and non-essential products pushed in this way. Tonics, for instance. It all begins with a free sample, but ultimately parents will starve themselves but not deny their children the once-free products they've been sold on. That's why I call medical representaives drug-peddlers : They are no better than the heroin peddlers of New York ! and after all, it's so easy to buy a doctor ! Slip him a few knick-knacks and he's in your pocket !"

Not so innocuous are the other methods used by medical representatives. Says an authoritative industry source who prefers to remain anonymous : "An occasional general practitioner may be bribed outright - he will be paid a lump sum of Rs. 10,000 to write out so many prescriptions of a particular brand in so many months, or to prescribe only one company's products. This of course is the crudest approach and there are many subtle variations on the same theme. For instance, out of every 100 boxes of a drug he orders, he may be offered 20 boxes free of charge. Or, for every 100 prescriptions of a certain brand, he is given so much of a 'cut'. Naturally, such transactions are virtually impossible to prove, though most pharmaceutical companies indulge in them at some time or the other, with or without the tacit approval of the higher-ups."

Another dubious method used to boost sales is the 'drug trials' gimmick. I talked to one such general parctitioner in Thane who, some years ago, had been one of a countrywide selection of doctors persuaded by a multinational to try out one of its broad-spectrum antibiotics, and to compare the effectiveness against another cheaper antibacterial substance. "Of course, I know the product was very good," he told me, "because it was, after all, marketed by such a famous 'foren' company." Were the studies he carried out on his patients double-blind ? I asked him (double-blind studies are about the only reliable way of testing a drug's efficacy and essentially involve neither

the investigator nor the patients knowing whether the drug itself or a dummy pill is being administered). The general practitioner, it turned out, had never heard of such trials. So much for 'tests show that.....is effective in 95 per cent of cases, and is the obvious choice.....', the standard, over-trumpeted claim in drug literature.

Often, however, such drug trials prove quite embarrassing to the manufacturers. Dr Antia remembers, "Sometime ago, we carried out studies at the J. J. Hospital in Bombay to study the effect of a drug for reducing facial swelling. We found that it was quite useless, but its makers prevented us from publishing out findings by invoking some clause in tiny print which we'd ommitted to look at."

However, gullibility and an itch to make a fast buck are not the only reasons why doctors fall for the viles of pharmaceutical firms. Often ignorance too plays a significant role. According to Dr UK Sheth, an eminent Indian pharmacologist and now a WHO consultant, "Once our doctors pass out of medical college and set up parctice, they are cut off from the world of pharmacology. Only those who are interested enough and find the time will keep themselves abreast of the latest developments in medical therapeutics – and these form a very small minority. The others are thus exquisitely vulnerable to glib medical representatives, who will often make it worth their while to prescribe their own products. This situation is quite different from that in developed countries like the USA and UK, where there are well-organised services rendering a constant flow of information about drugs to prescribing doctors. Thus we have a gaping lacuna in our country, and most firms take full advantage of it."

There is also a world of difference between the way drugs are advertised in the popular press (in the case of over the counter drugs) and in medical journals (in that of prescription drugs) in countries like the USA and India. Thus, in the USA the Food and Drugs Administration (FDA) insists on four requirements being met in every form of drug promotion : The ad must have enough information to enable the physician to use the product properly, including all known side effects, precautions, contraindictions, etc.; all such information must also be supplied on the labelling of the product ; equal emphasis must be laid on the good and bad aspects of the product, and finally the brand name must always be immediately followed by the generic name of an ingredient.

The situation here is appalling. How claims like 'Turns extra eating into extra growth' (Incremin tonic), 'Makes your blood redder and healthier' (Tonos-7) are allowed to be prominently advertised in the mass media is a mystery. "Even the ingredients nowadys are written in such tiny print that I often have to use a magnifying glass to decipher what exactly some new formulation contains! exclaims Dr Sheth

Shockingly, even medical journals in India seem to have become unduly lax. Dr R S Satoskar., Professor-Director of Pharmacology at Bombay's KEM Hospital, says "Of late, more and more ads are appearing in our medical journ-

als without the generic names being revealed at all. This is really a scandalous state of affairs ! "He pulled out a recent issue of the Journal of the Indian Medical Association, and showed me the ads of just two products, 'Calmpose' and 'Decaris'. "Nowhere in the entire full page ad is it mentioned that Calmpose contains Diazepam, and Decaris contains Levamisole. They say the dose is so many tablets per day, but so many tablets of what ? This is nothing but a trick to ensure brand loyalty. After all, they don't want doctors to know that there are a number of other brands of the same drugs, many of them cheaper than their own product. There are more than 40 different brands of Diazepam alone for instance".

Yet another gimmick employed in promotional literature is a 'reference' to medical authorities. Usually, these references are master-pieces of deceit, being lifted from their books or papers, twisted totally out of context, and juggled about to suit the promoters purposes. Dr. Satoskar, himself a victim of such a trick, recalls, "I have written in my textbook that emotional factors play an important role in menstruation, which is a perfectly true physiological fact. Some years ago, a pharmaceutical company marketed a new formulation containing an antidepressent and a sex hormone, citing my reference for its rationale. But I certainly did not mean to endorse such a ridiculous combination of drugs-far from it ! I promptly objected to the manufacturers and they had to withdraw my 'Reference".

It was in the wake of such rank unethical practices that the Kefauver Committee was set up in the US nearly a decade ago. Many of that country's stringent drug regulations stemmed from the committee's reports and recommendations. In a massive indictment of the pharmaceutical industry, the committee had concluded that "The high margin and profits in the drug industry result from monopoly control of the market exercised by larger firms, through monopoly grants that come from patents, through extraordinary high expenditure on promotion and advertising and their success in brainwashing doctors into writing prescriptions in terms of brand names, rather than generic names."

In India, the Hathi Committee report had suggested abolishing brand names of 13 essential drug formulations in an attempt to begin breaking this vice-like monopoly. These formulations included certain commonly used pain-killers, anti-anaemics, antibiotics, anti-hypertensives and anti-parasite drugs. In 1979, the government was reported to have decided to abolish brand names of just five drugs-analgin, aspirin, ferrous sulphate, chlorpromazine and piperazine salts-brand leaders of which are manufactured by multinationals. It came as no surprise that the move was stoutly opposed-not so strangely, Indian pharmceutical firms also resisted it-and it was quietly abandoned, at least for the time being.

Part of the reason why multinationals can indulge in such arm-twisting (methyl dopa, a drug for high blood pressure, is one of the most recent examples, but more of that later) is our crippling dependence on bulk drug imports. For, as the Hathi Committee reported, our imports in the decade 1963-64 to 1973-74 alone nearly tripled from Rs. 13.17 crores, to Rs. 37.50 crores. The next year saw a further hike to Rs. 47 crores, which constituted 35 per cent of the bulk drugs we

utilised in formulations. And after 1976, the noose has been getting tighter and tighter. As Dr. S. S. Gothoskar, the Drug Controller of India, said recently, "The last three years have witnessed a steep increase in the requirements of imported raw materials by nearly 100 per cent. Thus, while our production increased by only 50 per cent from 1976-77 to 1978–79 the expenditure incurred on import of bulk drugs, intermediates, solvents, etc., rose by nearly 80 per cent." Until this dependence is eliminated, or at least significantly reduced, multinationals will continue to thwart any attempts by the authorities to introduce urgently needed drug legislation.

Health Drinks

The Government's recent decision to appoint a working group to devise means for halting the cancerous proliferation of baby foods in the country though long overdue, is a step in the right direction. Unfortunately, the foibles of the closely related health drinks industry have not apparently been brought to the attention of the powers – that–be yet. Meanwhile, for about half a dozen companies including two multinationals which together manufacture about 15,000 tonnes of health foods annually in India, it's business as usual.

Leading the field is Horlicks, a product of UK's Beecham International, which got off to a head-start in the country through its subsidiary, Hindustan Milkfoods Manufacturers (HMM) in the early fifties, though it was imported for more than a decade before that from England. Today Beecham holds 60 per cent of the equity and is reportedly going to relinquish a further 20 per cent 'soon' to the Indian subsidiary. Of the total health drinks market in India, estimated at around Rs. 43 crores a year, Horlicks now corners about 53 per cent. Moreover, five years ago, it launched Boost a brown alter ego of Horlicks, which is a 'white' drink. Backed by an assiduous ad campaign, said to cost its makers some Rs. 25 lakhs a year, Boost has now managed to acquire another 7 per cent of the total food drinks sales, giving HMM the lion's share (60 per cent) of the Indian market. Trailing far behind Beecham International and its subsidiary. HMM, is yet another UK–based multinational, Cadbury. The company, which markets Bournvita, besides a number of other chocolate products, currently corners about 25 per cent of the health drinks market in the country.

The answer to the Big Two's hold on the industry lies only partly in their high–pressure ad programmes : industry insiders claim that both the companies together account for about Rs. 1 crore of the nearly Rs. 1.75 crores spent in all by the country's food drink makers on advertising.

Recently, an exhaustive survey carried out by UK's Social Audit revealed, among other things, how both Horlicks and Bournvita are promoted in markedly different ways in two countries. In the UK these products are promoted as 'mild soporifics'. In fact, Bournvita's advertising copy highlights it as 'A Goodnight Drink' which 'helps sleep come naturally'. Again, in sharp contrast to India, the Bournvita tin in Britain bears no blurb about it being 'the ideal health drink for strength, vigour and taste'. So is the case with Horlicks too, which is sold in the Uk as 'the ideal food drink of the night....helps you relax into the proper

rhythm of sleep; helps nourish you through the sleeping hours until you wake restored...' Compare this with the well-known 'Suchitra' ad which appears regularly in leading Indian magazines and papers, in which the copy reads, 'Horlicks the Great Nourisher... builds resistance, safeguards health day after day.' In magazines like Sportsweek, the great nourisher is going to transform Raju into 'another Pele'. Strange how such a galvanising elixir in India becomes a soothing 'goodnight drink' in the UK!

When I met Mr. D. Shourie, Cadbury India Ltd's marketing manager, I asked him if he knew of the difference in the promotion of Bournvita in the two countries, and if he could explain it. He first said that he did not know how Bournvita was advertised in the UK, and then hastily amended it with a "I would't like to comment". When I then asked him if he could justify Bournvita's most prominently advertised claim–the one referring to extra energy, strength, et al - he smiled patronisingly and asked me if I had seen any recent ads of Bournvita; his way of telling me that Bournvita was at present being promoted as the 'Olympic' drink. So I asked him if Bournvita's 'energy' claims were going to be totally discarded or whether they would stage a comeback with the passing of the Moscow games. To which also Mr. Shourie replied with "I don't know". By a queer coincidence my attention was drawn the very next day to a new Cadbury Drinking Chocolate ad featuring that product as the 'Perfect Goodnight Cup'. One wonders whether this heralds the transition of Bournvita from an energiser to a soporific in India too...

Actually, in recent years, the government has pressurised the promoters of these two brands to tone down their more extravagant claims. Till a few years ago, for instance, Horlicks was advertised in India 'twice as good as milk', a patently untrue blurb dropped at the insistence of the government. Not so apparent, points out Social Audit's study has been the conversion of 'Bournvita gives children all the precious nourishment they need' to 'Bournvita helps to provide them with all the extra energy they need', to again, till as recently as 1975, as stressed the usefulness of Bournvita as a 'brain food' – I want my little girl to be more active healthier and smarter. So I give her 'Bournvita every day'.

The Social Audit investigators discovered that over the year, the promoters of Horlicks had perfected an ingenious system of utilising the medical profession as pawns in the marketing game, particularly those, like general practitioners and paediatricians, who can provide an easy conduit to growing children. In most urban areas they had apparently made up lists of general practitioners and consultants according to their type of practice. Special 'Medical Sales Forces' were employed, consisting of company representatives, whose major function was to visit these doctors at least once a year, and even upto four times a year, the frequency varying with the size of the practice. Medical personnel and administrative authorities of large government hospitals were also reported to be subjected to this barrage of visits.

Of course, in addition to this personalised promotion of their product, HMM also relied on another time-tested technique : Sponsoring conferences, seminars and programmes for doctors as well as would–be doctors (medical students and interns). HMM had even been known to donate TV sets to patients and

nurses in hospitals. Naturally all these gifts bore the stamp of 'Horlicks' and more than adequately got the message across to the consumer.

Unlike Horlicks, Bournvita does not depend on the co-operation of doctors to be sold–not yet anyway. But according to the Social Audit report, an attempt was made a few years ago to enlist doctors' help in promoting Bournvita, and it had proved a damp squib. The trial was apparently undertaken in the West Bengal area, where Bournvita usually does not sell as well as Horlicks. However, it failed not because of the doctors dragging their feet, but because of consumer resistance to switching over from Horlicks. Milk was rather scarce there, and is needed for a drink of Bournvita, while Horlicks can be prepared without it. Horlicks had thus become too firmly entrenched in the sector to be dislodged by Bournvita.

None of the above findings and conclusions were refuted by either HMM or Cadbury India. In fact, Social Audit was told that in the last decade or so, the sales of Horlicks all over the country had more than doubled. Horlicks costs much more than it does in the UK, and obviously the sole factor responsible for this is the popularity of the brand, even though sources at Beecham International claimed that this was due to higher production costs and taxes in India. What is more, Social Audit were proudly told that the Indian sales of Horlicks would soar upwards by another 50 per cent in the next five years or so, and of course there will be a corresponding increase in prices.

While Horlicks concentrates on the medical profession, its major competitor Bournvita utilises the captive audience of school children for its promotion in quite a subtle manner. Its manufacturers sponsor popular children's activities that include a general knowldge quiz on AIR, and an annual school sports meet. Recently, Cadbury India-received the status of 'official suppliers' to the Indian contingent of the 1984 Olymics and with these fact approaching, Cadbury has launched a new ad campaign, featuring Bournvita as an 'Olympic' drink - again, stressing like it has been doing all along, what Charles Medawar of Social Audit terms the highly questionable connection between Bournvita and strong bodies and minds.

Falling in the same category of products is Glaxo's Complan, advertised as 'the complete health drink...has scientifically planned proportions of protein, carbohydrates, minerals, vitamins and other vital foods everybody needs, every day, for fitness and energy. Just the thing for elders in the family, who aren't well enough to eat. For busy husbands who are often too rushed to eat. For fussy children who simply refuse to eat. For you, when you're too tired to eat.

Each 100 gms (slightly less than half a 250 gm tin, which means about Rs. 10 worth) of Complan contains 20 gms of proteins, 16 gms of fat and 55 gms of carbohydrates. Since 1 gm of both protein and carbohydrate each yield about 4 calories in the body, and 1 gm of fat about 9 calories, 100 gms of Complan will give about 350 calories.

Now let's examine each of Complan's 'uses'. Take the one about it being 'just the thing for busy husbands who are often too rushed to eat' unravelling this gem of ambiguity presents a problem. One wonders whether Co-

mplan is just the thing for hubbies who are perennially too busy to eat any meal, that is, or just one meal a day.At any rate,let's presume Complan is just the thing for hubbies who miss one square meal of their two daily meals, Since an average Indian male, doing moderate work, requires, according to the ICMR, about 55 gms of protein and 2800 calories, such busy husbands missing one meal every day, should get about 30 gms of protein and 1500 calories 'extra'. Now the whole 250 gms tin gives only about 25 gms of protein and 1200 calories, so that even if they consumed it whole, they still wouldn't be getting enough protein and calories ! And the tin advises 33 gms of Complan twice a day, which will provide only about 13 gms of protein and 300 calories. Just three cups of coffee or milk also provide roughly these many calories.

Not to be outdone by the Multinationals, local manufacturers too have begun operations on the food drinks market. Of the various brands jostling for about a fourth of the market, Nutramul, a health drink from the makers of Amul, seems to have got off to a good start on its competitors. Launched in 1975 with a well-organised ad campaign which industry sources claim costs its makers more than Rs. 15 lakhs annually, Nutramul has managed to annexe about 5 per cent of the total market, good going for five years, considering the competition it faces from the established brands. Again, like Bournvita and Horlicks, Nutramul also tries to cash in on the healthy body-food drink concoction : Its ads are usually geared around the current craze for martial arts.

"Needless to say," points out Dr. Satoskar, "the claims of all these products will not stand a close pharmacological scrutiny.All they provide is an expensive means of adding colour and sweetness to milk, which even a few drop of essence can do. At any rate, they concentrate on children of the upper strata who are fussy about drinking milk – a ridiculous fad insidiously nurtured by some of them. (Nutramul's ad, for instance, goes – 'Raju hated drinking his milk.....Now he's a Nutramul dada,) Unfortunately, however, their heavy promotion has even hooked those parents who cannot really afford them. Their children would be much better off with much cheaper and more nutritious foods!

Tonics

Waterbury's Yellow Label Tonic is one of the brand leaders in this multihued, multiflavoured market. The exuberant blurb exclaims, 'Here's bubbling health and extra energy for your family!' What extra energy means, and how exactly Waterbury's tonic provides, it is anybody's guess. 'Waterbury's is a balanced formulation of vital ingredients,' goes the ad copy, 'With vitamins and minerals for growth and energy. Iron to build healthy blood. Stiumlants for appetite. And it tastes good too.' In fact, each teaspoonful of Waterbury's contains just 3 mg of iron, of which only about a tenth may be actually absorbed by the body. How this miniscule amount will 'build healthy blood' is a mystery, considering that the ICMR recommends at least 10 mg of iron daily for men, and 20-30 mg for women. And the men and women at whom this ad campaign is directed certainly look like

they consume a diet containing at least that much iron. As for that bit about 'stimulants for appetite' the reference is obviously to Waterbury's 10 per cent alcohol content – a figure remarkably similar to the alcohol contents of dozens of other tonics, which also claims to be appetite - stimulants. The appetising effect of alcohol has been really cashed upon!'

Many tonic manufacturers have jumped on the iron bandwagon. Femibon goes a step further : It is a tonic meant exclusively for menstruating women, whom it unnecessarily alarms with dire warnings like, 'Doctors say that as a woman you need twice as much iron as man. And here's what happens if you don't get it.....you could start feeling tired, irritable and unable to give your family all the love they need. Your daily diet does not normally provide this extra iron you need.' Ironically enough, the diets of most women who are Femibon's targets do get enough iron in their diet, but those who don't (iron deficiency anaemia is extremely common in India, especially among the lower socio-economic classes) cannot afford Femibon, Which is probably all to the good, because there are much cheaper formulations providing more iron than Femibon. And at any rate, it would be harmful if such women consume tonics like Femibon. For as Dr Modell warns, "There have been reports of serious consequences of suppression of early signs of anaemia because of the subclinical doses of haematinics (drugs such as iron and vitamins) used in such mixtures,"

Another tonic, Incremin, is pushed with the banner, 'A tonic that just increases appetite is only doing half its job (sic). Get Incremin - it turns extra eating into extra growth, because it contains an important amino acids that makes better use of the proteins your child eats.' No medical authority will even attempt to explain the ridiculous claim about Incremin turning extra eating in to extra growth. Of course, it depends on what the manufacturers mean by growth - if they mean girth, it's fine The not–so–subtle attempt to play upon parental concern, however, is based on a half-truth. Each teaspoonful of Incremin contains 300mg of lysine, an essential amino acid, essential because the body cannot itself synthesise it. But even a handful of peas will provide more than six times this amount of lysine-and peas are considerably cheaper than Incremin. Besides, the other constituents of Incremin are just a waste of money–10 times more vitamin B I than is needed daily, 25 times more vitamin B 12 and twice that of vitamin B 6.

Yet another gimmick dreamt up by tonic manufacturers is the 'phosphates, theme. Essentially, this consists of having a basic hotch–potch of vitamins and iron (in the usual bizarre doses of course) and sprinkling an assortment of phosphates into it. Neurophosphates, Hemiphos, BG Phos are only some of the tonics based on this. Apparently they have all been inspired by the fact that nervous tissue consists mainly of combinations of phosphates and fatty substances called phospholipids. Extrapolating it in a tremendous exhibition of marketing ingenuity, Waterbuty's ads till some time ago used to claim that it contained 'phosphates to tone up your nervous system'.

The Common Cold - A Hot Market

Cold 'remedies' may be roughly divided into two types–the rubs (ointments) and oral medications (tablets, capsules, discs, etc). In the rubs market, Vicks Vaporub and Rubex together account for more than 50 per cent of the sales. A comparison of their contents reveals the astonishing fact that both contain nearly the same ingredients in the same percentage. As for effectiveness in colds, three of their constituents, camphor, menthol and turpentine oils, act as 'counter-irritants'-chemicals that, when rubbed in, increase blood supply to that part and warm it. Paraffin oil is an emollient, a substance facilitating application over the skin, while eucalyptus oil is a counter-irritant, and nutmag oil a flavouring agent. Conceding that rubs are 'a good gimmick' Dr Sheth says "People fall for the warmth, tingling and vapour that the volatile oils contained in them generate when rubbed in-after all, when you take a tablet you don't feel anything!' Needless to say, no controlled clinical trials have ever been undertaken to prove the efficacy of these ointmens in treating colds."

Among the oral cold remedies, many brands like Coldarin and Vicks Action 500, make much of their decongestant properties. Coldarin in fact puts it first in its list of claims : 'A decongestant to clear runny nose and sinus' goes the ad copy. While Coldarin contains a drug called phenylephrine, Action 500 has another called ephedrine, both belonging to a class of drugs termed sympathomimetic amines, which given by non oral routes, can cause constriction of blood vessels. These drugs are not given orally because they are not well – absorbed, and are usually administered in the form of drops so as to cause local decongestion. And, as Goodman Gillman's The Pharmacological Basis of medical Therapeutics puts it, "No convincing evidence of benefit from oral use of (such drugs) to relieve nasal congestion in colds has yet been presented."

"Not only are these drugs of dubious value as nasal decongestants when taken orally," says Dr Satoskar, "but they may also prove positively dangerous. For instance, if an elderly man suffering, from hypertension is being treated with a certain class of antihypertensive medcations, there can be an interaction between the two drugs and a dangerous rise of blood pressure may result."

Another constituent of such 'blunderbuss' preparations (as Goodman Gillman calls them) is an anti–histamine. Brands like Vikoryl, for instance, contain such drugs. "Needless to say, such anti-histamines are useless in the common cold. Occasionally, however, in cases of allergic rhinitis, they may prove effective, and thus the patient is deluded into believing that the preparation 'worked' against what to him was a cold. A more dangerous effect of such drugs is that they dry secreti secretions in the respiratory passage–ways, causing them to go into spasm," points our Dr Satoskar.

Yet another addition to the endless cold pharmacopoeia is Vitamin C. Thus, Coldarin is specifically advertised as 'The Special Cold Tablet With Vitamin C.' Vitamin C (50 mg per tablet) is claimed 'to build up resitance'. To what ?, one is tempted to ask. The cold viruses ? A laughable claim indeed. All

that 50 mg of Vitamin C is going to achieve is a big zero–most of it will be excreted next day in the urine. And if the manufacturers are trying to cash in on the Vitamin C controversy sparked by Dr Linus Pauling, they prefer to ignore the fact that he advocates grams of it every day to abort colds, and not a measly 50 mg.

Thus, the dozens of cold tablets and capsules available on the market are merely expensive brands of aspirin to which have been added permutations and combination of a number of other drugs that are either harmful (phenacetin), useless (Vitamin C, anti-histamines) or ineffective (pheylephrine, ephedrine).

Another class of Products heavily promoted for colds are 'cough drops, which come in an astonishing variety of sizes, shapes, colours, tastes, and of course prices. Only a careful analysis of their contents shows how useful (or rather useless) they actually are. Consider Vicks Cough Discs, Halls and Strepsils, which between them share most of the market.

Each Vicks disc contains about 3 mg of a drug called dextrometnorphan, 3 mg of ephedrine, besides about 5 mg of menthol. Dextromethorphan is an antitussive (cough-depressant) while ephedrine helps in widening the bronchial Passage–ways to enable expectoration. But, according to pharmacological authorities (Satoskar, Kale, Bhandarkar, Modell), their minimus doses are 15 mg each. Therefore, at least six Vicks discs would have to be popped in at a time for the minimum dose to be ingested.

The third ingredient, menthol, is also utilised by other brands (Halls, for instance, with the claim, 'Clears Stuffy Nose'). To quote Drill's pharmacology in Medicine, "Menthol when applied locally causes a pleasant tingling sensation and a feeling of coldness. These changes which are probably due to the result of an effecf on the sensory nerve or nerve–endings have led to the use of menthol in a variety of proprietory drops liniments and cigarettes." Eucalyptus, a substance similar to menthol, is Halls' second ingredient and is equally ineffective in treating colds.

The manufacturers of all these products stress their 'soothing' action but what they do is just increase the secretion of saliva. And according to Dr Sheth, "A bit of Khadi shakhar, which our mothers used to give us, is as good. After all the object is to prevent a drying up of the throat mucous membrane, which brings on coughing. This purpose can be served equally well by a piece of sugar, candy or lemon drops–and at much less cost than the heavily advertised throat soothers and cough discs."

To quote Drill again, "These variously-shaped medicated candies....contain sugar and mucilage, besides the active ingredients which are mostly antiseptics or antibiotics, menthol and local anaesthetics. They are generally considered to be of dubious value and the US pharmacopoeia does not contain any such preparation....." And in India, just one such 'medicated candy', Strepsils, is worth more than one crore rupees to its maunfacturers every year.

Sex Hormones

Certain estrogen–progesterone mixtures, administered to test whether women who missed periods are pregnant or not, have long been indicted on two important counts: one, that they do not constitute a realiable test on pregnancy (after all,

there are cheaper and surer methods of detecting it) and two, that they are very likely to produce a number of deformities in the unborn body. These hormone mixtures have been banned in a number of countries abroad (Sweden, Finland, US, Singapore, UK) but till some time ago, they were freely sold in the Indian market, many of them without even a statutory warning.

Last April, Dr B. Palaniappan, Professor of Gynaecology and Obstetrics at Madras Kilpauk Medical College, publicly decried the use of such combinations, claiming that a study he had conducted had proved their dangerous potential. A campaign to ban them followed in certain sections of the Indian press, questions were asked in Parliament, and the drugs have now all begun carrying the innocuously worded warning : "There is some evidence to show that hormonal preparations when used during pregnancy may lead to foetal abnormalities and as such, these should not be used during pregnancy or for pregnancy diagnosis unless a decision has been taken to terminate the pregnancy after its confirmation." Obviously, while this is better than nothing, such a 'warning, merely begs the question, and can have no better effect than the statutory warning on cigarette packs. Only a ban on such combinations will prevent their misuse.

Another group of sex hormones that has recently hogged the limelight in the US consists of long-acting progesterones. One such drug, called medroxy progesterone acetate, marketed by Upjohn under the brand name Depo Provera, was banned by the FDA some time ago because of reports of its side-effects including what one medical journal called 'menstrual chaos', cancer in experimental animals, and even prolonged and permanent sterility. After more than a decade of girm struggle with the FDA, Upjohn was forced to withdraw Depo Provera from the US market, but in classic 'dumping' style, the drug has been unloaded on a number of Third World countries. In India, a closely related long-acting progesterone, called 17 alpha hydroxy progesterone caproate, is commonly used. One brand leader, Proluton Depot, marketed by Scherring is specifically promoted as follows : "Proluton Depot should only be prescribed if there is an urgent desire for children.....It is indicated for both prophylaxis (prevention) and treatment of abortion.....To achieve an effect to maintain pregnancy, a prolonged treatment with an adequate dosage of Proluton Depot is necessary....."

The manufacturers slickly circumvent incrimination of sex hormones in causing foetal defects bysaying : "A possible association between the administration of female sex hormones in early pregnancy and the occurence of malformations has been the subject of discussion in recent years. According to the present state of medical knowledge, the assumption that there may be a casual relationship can be regarded as unfounded." Does this mean that there is something seriously wrong with 'the present state of medical knowledge, the assumption that there may be a casual relationship can be regarded as unfounded." Does this mean that there is something seriously wrong with 'the present state of medical knowledge in countries like the USA and UK, which

have banned such drugs for this very reason, and which Scherring would have us believe is an ,unfounded assumption'?

The literature further goes on to say, ''However, it must be clearly understood that no drug, including sex hormones can be claimed with absolute certainity to be free from teratogenic effects. This remaining uncertainty is the reason why in certain indications, the exclusion of pregnancy is called for before the start of sex hormones therapy.....'' A classic example of double-talk'.

''No one knows the true effects of long-acting progesterones on the uterus, says Dr Satoskar,''and no one is sure that they help in preventing threatened abortion too. Yet they are routinely used in such cases. Who knows what risks such women are exposed to ? More shocking is the experimental use of these drugs as long-acting contraceptives, which I believe is still going on in some Indian centres.''

''Yet another perturbing feature of hormone use,'' says Dr Satoskar ''is the indiscriminate prescription of so-called tonics containing drugs called anabolic steroids. These have been enthusaistically promoted for all kinds of patients from the young child who does not seem to be growing well to its doting parents, to older men and women desperately desiring to regain their lost youth and vitality. I have seen a number of children with precocious sexual development, who had been given these tonics months on end. Then there was an older female patient who came to me with an embarrassing problem-excessive hirsuteness and an incipient beard. I found that she had been drinking one of those tonics for a long time. In the US, tonics containing anabolic steroids like stanzol are prohibited for routine use as appetite-stimulants because they are known to have adverse effects on the physical and sexual growth of children. Yet in India, a number of them are pushed with claims like, 'Improve the appetite', 'Imparts strength and vigour', 'Restore a sense of well-being'.....''

Pain-Killers

Three dangerous pain-killers-analgin, amidopyrine and phenacetin-are still commonly used in India. About the first, the American Medical Association categorically states, ''Because Dipyrone (analgin) may produce fatal agranulocytosis and other blood dyscrasias, its use as a general analgesic, anti-arthritc or routine anti-pyretic cannot be condoned. Its only justifiable use is in serious conditions (for example, febrile convulsions in children) in which a parenteral anti-pyretic preperation may be needed after other measures like sponge baths and other drugs failed, or rarely in malignant diseases for instance Hodgkin's. when fever cannot be controlled by other means.''

But in India, Hoechst claims that its product Novalgin, ''is a potent non-salicylate analgesic, anti-pyretic, anti-spasmodic, anti-inflammatory and anti-rheumatic agent indicated for all types of pain, relief of rheumatic fever and rheumatoid arthritis, and relief of colics''. ''In febrile conditions due to any origin, the temperature rapidly reverts to normal following Novalgin,'' it says. There is only one point of caution besides an allergic reaction that the literature mentions : Although the danger of agranulocytosis is remote it has to borne in mind and a white cell

count should be done if the general condition of the patient so warrants." In marked contrast is the US Label for Dipyrone which carries a mandatory warning that it "should be restricted for its anti pyretic effect in serious or life-threatening situations."

Over 90 brands of this drug are sold in India, which gives some indication of the extent and lucrativeness of its market. "Unfortunately, "says Dr Satoskar, "because of intensive promotion this dangerous drug is now being routinely used in our country. Laziness on the part of some doctors is also responsible for this. They want to impress their patients ; they don't want to wait for plain aspirin to bring down their fever. After all' an injection of Novalgin is a much better money-spinner than a few tablets of aspirin."

At least 50 per cent of aplastic anaemia cases reported nowadays are due to this drug." he claims. "Its rate may be one in 1000 or one in 100,000 we just don't know, but for that one person the rate is 100% and such diagnoses are made only in cities like Bombay, where facilities for the recognition and confirmation of a disease like aplastic anaemia are available. Who knows how many deaths this drug causes in the remote areas of rural India, where too the aggressive promotion of analgin has percolated". After all, the analginh market in India is worth some Rs 5 crores annually.

Another pain-killer amidopyrine (chemically closely related to analgin) has also been known to cause a number of dangerous side-effects. The drug is now nearly a century old, and its OTC sale was banned in the US as far back as 1938. Following reports that it caused a fatal depression of the bone marrow and also perhaps stomach cancer, the World Health Organisation recommended its withdrawal from routine therapeutic use. Many countries like Switzerland West Germany, Japan, USA and UK, have now banned the drug. A few years ago, the Indian Council of Medical Research carried out studies on amidopyrine, and while accepting that it is incriminated in stomach cancer and bone-marrow suppression, only recommended that it be withdrawn from the market in a phased manner. This reluctance to ban it outright was perhaps motivated by the fact that the country's analgesic production was not sufficient to meet domestic demands then.

Some time ago, the Maharashtra FDA decided to ban 'Esgipyrin', a combination of amidopyrine and phenylbutazone marketed by Suhrid Geigy. But the FDA in other states, like Gujarat, did not ban it. Therefore the manufacturers claimed that this was discriminatory and obtained a stay order on the ban. The Maharashtra FDA's appeal has still to be heard so that amidopyrine's fate in India will not be known for the next few months at least,

Yet another pain-killer banned in certain countries, but still extensively used in India, is phenacetin. Pharmacologists all over the world have documented enough evidence that its continued used in large amount leads to kidney damage and failure. Dr. S. R. Amladi, Professor of Pharmaco-

logy at Bombay's BYL Nair Hospital, points out "There should be no place for phenacetin in therapy today because after all it is mainly converted to paracetomol in the body, and it is this paracetomol that exerts the pain-killing action, while the other by-products have a toxic affect." Which makes nonsense of phenacetin manufacturers' claims that "instead of blindly aping the West, the government should investigate the use of phenacetin in all aspects before banning this useful and essential drug (emphasis mine). At any rate, the phenacetin lobby is apparently quite strong because it is still freely available and used, inspite of the authorities' reportedly 'thinking of banning it for quite some time now.

Dozens of analgesic mixtures are sold on the Indian market, each containing besides aspirin, either phenacetin or caffeine or both. While phenacetin should not be used, caffeine is useless in the doses the mixtures contain, so that they are merely expensive variations of aspirin with perhaps less pain-killing but more dangerous potential than simple aspirin (Aspro, Anacin, Codopyrin, Cafiasprin, Dodalgin, Dristan Daprisal, Veganin, Verindon, to name a few such mixtures). As Goodman Gillman says, "The many mixtures of aspirin with phenacetin and often with caffeine and other drugs are promoted with claims that they provide greater analgesia and/or cause fewer side effects than does aspirin alone. Neither claim withstands critical scrutiny. In most controlled clinical trials, relief of pain by an analgesic mixture has not been superior than that of aspirin alone. In the occasional trial in which a mixture has provided somewhat greater pain relief, the difference has been of doubtful significance, or aspirin would have probably been as effective if it had been employed in comparative dosage.

"Caffeine is included in many suuh mixtures, presumably in the belief that it increases the anlagesic effect in general, has unique value for relief of headache and exerts a favourable influence on mood. In patients with cancer the analgesia provided by aspirin 650 mg is not increased by concurrent administration of caffeine 65 mg. In controlled trials analgesic mixtures containing caffeine have not been found superior to aspirin for relief of headache nor has caffeine been shown to contribute other favourable effects. It is pertinent that the dose of caffeine employed for relief of migraine, with ergot alkaloids, is 100 mg, and that a cup of coffee contains 100 to 150 mg of caffeine ; yet the caffeine of the usual analgesic mixtures is only 16 to 65 mg.'

Antibiotic Abuse

Chloramphenical, a broad-spectrum antibiotic, ran into difficulties in the US because of aplastic anaemia, a rare but usually fatal side effect. However, the many manufacturers, among them Parke Davis, the brand leaders, soon found a way out. Pharmacologists are agreed that its main use is in typhoid, but to quote the American magazine Mother Jones (November 1979) "the problem (for the drug firms) is that there are only a few hundred cases of typhoid a year in the US. Hence Parke Davis for many years aggressively pushed its Chloromycetin as a cure for a wide variety of other maladies. Experts testifying some years ago before Senator Gaylod Neloson's small Business Subcommittee on Monopolies said that

between 90 and 99per cent of Chloromycetin prescriptions were being given out for common colds, acne or other conditions for which no drugs are effective or other drugs are safer.

"Eventully, under the pressure of congressional hearings, lawsuits and other publicity, chloramphenicol sales in the US declined sharply, Parke Davis began printing warnings on Cholorom-ycetin packages sold in the US stressing that the drug should only be used for a few life-threatening illness. Are these warning 'Justifiable'? Senator Nelson asked Parke Davis executive Leslie Lueck at a 1967 hearing. 'Yes,' he replied. To Lueck's consternation, Nelson than produced an ad for Chloromycetin from the British Medical Journal The Lancet that carried no warnings at all. Lueck made some excuses ; Nelson said 'I don't see how you people can sleep at night.'

If Parke-Davis people lost any sleep over Britain, they ought to have become insomniacs over Latin America. There University of California pharmacologist Dr Milton Silverman reported in a 1976 study, that chloramphenicol was recommended to physicians for treatment of all sorts of conditions–including tonsillitis and bronchitis–that were scarcely life–threatening. Parke Davis gave no warning at all about the drug to doctors in Guatemala, Costa Rica and other Central American countries. McKesson Laboratories, a rival supplier of chloramphenicol, recommeneded its brand for whooping cough ; while it disclosed a few hazards to doctors in Central America, it listed none at all in Ecuador and Colombia.

"Besides causing an unknown number of deaths from aplastic anaemia, promiscuous use of chloramphenicol-like that of many antibiotics has had a more serious consequence : bacteria have built up resistance to it.

"No one knew how serious a problem this would be until a 1972–3 epidemic of typhoid fever in Mexico. Believed to be the most catastrophic outbreak of typhoid in history, it afflicted about 100,000 people. Up until that point, most doctors had assumed that chloramphenicol would prove as effective against typhoid as it had in the past. To their dismay, they were wrong. The particular typhoid bacteria they were dealing with had, through long exposure, built up resistance to chloramphenicol. Doctors were largely helpless.

"20,000 of the typhoid victims died."

Chloramphenicol - resistant typhoid germs have been reported in India, though fortunately, no massive outbreak like the one in Mexico has occurred—yet. Such resistant bacteria were first reported from Calicut in 1972. In succeeding years, other towns in South India have also reported resistant bacteria. In 1976, they appeared in Bombay. Already, the ICMR has been seized of this grave development, and has warned that "if urgent action is not taken, it will only be a matter of time before drug-resistant typhoid fever spreads throughout the country".

In the USA the FDA permits only two absolute uses for chloramphenical–typhoid fever and a dangerous infection with a bacillus called Haemophilus influenzae. In India it is advertised among physicians for a

multitude of others. For instance, here is an extract from Boehringer Knoll's Therapeutic Index : "Indications-Typhoid and paratyphoid, Bacillary dysentery, Amoebic dysentery as an adjuvant along with the amoebicide, Whooping cough, non-tubercular respiratory infections especially of the chronic and recurrent type, Urinary infections, Surgical infections, Wound infections, Burns Ricketssial infections, Infections resistant to other antibiotics and chemotherapeutics ..."

Another recent development in the US has been the FDA making it mandatory for chloramphenicol preparations to print 'may be ineffective when injected intramuscularly' on the package. (Texts like Goodman Gillman have said the same thing for a long time now). Such injections of chloramphenicol are quite common in India, particularly for cases of gastroenteritis. "But," says Dr. Satoskar, "Most such cases are self-limiting-either viral' allergic or irritant. Obviously chloramphenicol is useless for the first two, and the third will only be cured when the irritant is excreted. So the intramuscular injection of chloramphenicol in these cases does not make any sense. In India, chloramphenicol should be restricted to the treatment of typhoid and paratyphoid. Because of its adverse effects, it should not be used primarily as a broad-spctrum antibiotic.',

Tetracyclines constitute another much abused group of antibiotics. They should not be used in children below eight, because they cause discolouration and disordered growth of teeth in them. Yet the market of tetracycline drops in India is worth approximately Rs. 5 crores, an index of its widespread use in this vulnerable age group.

Multivitamin Mania

Vitamin combinations come in two main categories - B complex and multivitamins. A careful study of just two brands in the hundreds of B complex formulations sold on the market reveals how the consumer has been hoodwinked into buying these expensive and usually unneccessary products. Surbex-T, for instance, contains 15 times more vitamin B 1 than is needed 10 times more vitamin B 2, 5 times more vitamin B 3,5 times more vitamin B 6 and twice the amount of vitamin B 12 required daily (all based on the recommendations by the Indian Council of Medical Research). And as for Becosules, the amounts exceed the recommended daily requirements by factors of 50, 12, 5 and 5 respectively.

The tragdy is that patients as well as physicians have been sold on the vitamin line through a well-orchestrated promotional campaign. As Dr. Satoskar puts it, "People have been made to believe in the need for extra vitamins."

"Take executives, for example – the one class at whom most of the vitamin ads are directed. Their diets undoubtedly provide them with more than adequate amounts of nutrients so that they can have no real vitamin deficiency. Their only problem is the terrific strain they are constantly exposed to and the tension that occasionally manifests itself in the form of psychosomatic illness like headache, bodyache, etc. Such people are easily persuaded to believe that their

problems are due to nutritional or vitamin deficiency. Naturally, they are also made to believe that there's a quick and easy solution to these problems – just a multivitamin capsule a day ! Little do they realise that the B complex vitamins they're paying through their nose for are all flushed from their systems in the next one or two days !''

Doctors too appear more than willing to encourage this gullibility. Willingly or unwillingly, they have jumped onto the multivitamin handwagon. Dr. Walter Modell, the eminent American pharmacologist and author of 'Drugs of Choice', a yearly publication enjoying immense status in the medical commnity, minces no words while discussing this sordid state of affairs. ''Partly to be doing something, partly to remove the pressure and relieve himself of his guilty feelings of incompetence or impotence, the physician may use vitamins by default: 'I don't know what to do. Vitamins won't hurt. Let's try some vitamins'. The body reacts to large amounts of vitamins as it does to poisons, by eliminating them in the urine, by inactivation or chemical decomposition. We do not yet know whether large amounts of a single element of the B complex produces imbalance. We do know that fat-soluble vitamins A and D, if taken too long in large doses, produce serious or even fatal intoxication or chronic illness.''

Warning against 'the notion of supercharging mood and physical capacity through eating added vitamins' (which almost all such brands subtly or blatantly claim to do) Dr. Modell says, ''This is really analogous to loading an automobile with 500 gallons of gasoline or 50 times the optimal amounts of tetra ethyl lead just because at a certain stage it improved things. The notion that if some is good, more is better, is a dangerous partial truth.''

Cost, of course, is of no account in chasing this mirage. In fact the costlier the vitamin pills, the more pronounced is the obsession to swallow them. As a busy general practitioner in Matunga told ''Whenever I prescribe a cheap brand of multivitamins (which usually implies a less well-advertised product) the patient comes back saying 'they don't work'. But give them the most expensive brands, which they themselves insist upon, like Surbex-T, and they're happy !''

Some time ago, the authorities had decided to force some semblance of sanity in the marketing of vitamins in India by permitting the sale of only two categories of formulations termed 'therapeutic' and 'prophylactic'. 'Therapeutic preparations were to contain amounts that are used to treat specific disease, due to vitamin deficiency (for instance, 50 mg to treat a disease called beriberi, caused by lack of vitamin B I) while the 'prophylactic' ones would contain just enough vitamins to prevent their deficieneies arising,and would thus conform to average daily requirements (for example, about 1 mg vitamin B I, as recommended by the ICMR). The FDA in America has somewhat similar guidelines to regulate the sales of vitamins in that country. Introduced in the early seventies, the measures have certainly

helped to eliminate the wasteful and expensive abuse of vitamins in the US.

Accordingly, multivitamin manufacturers in India are reported to have submitted their new price lists for the two categories to the Ministry of Petroleum and Chemicals. The Ministry was supposed to grant price approvals by December 1978. For reasons best known to itself the deadline was progressively postponed from then to July 1979, then to September 1979, and finally to December 1979. Since then, however, the Ministry has maintained a mysterious silence over the whole subject, prompting doubts that the whole matter has been indefinitely shelved.

Meanwhile, it's business as usual for the multivitamin marketeers, "I don't know why the authorities are dragging their feet about introducing this essential piece of drug legislation," laments Dr Satoskar. "There must be a powerful lobby behind it." He could be right—after all, a study by the Economic Times a while ago revealed that there were 68 companies that would be affected by the new legislation, of which as much as 24 were multinationals. Of the incredible number of multivitamin formulations that have flooded the Indian market (571 at last count, according to the same study) almost all would have to be reformulated, at a cost of Rs. 1.5 crores to the manufacturers. Enough reason, surely, to delay things as far as possible!.

Arm-Twisting in Bulk

The tongue-twisting alphamethyl dopa, a potent drug used for reducing high blood pressure, provides a glaring instance of how multinationals can virtually hold Third World countries like India, with inadequately developed pharmaceutical resources, to ransom. The brand leader of this drug market is Aldomet, marketed by the US-based Merck Sharpe and Dohme. Some time ago, the government of India and MSD got into a wrangle over who should procure the bulk product before MSD formulated and marketed it: On the one hand, MSD insisted on getting it from its parent company in the US, claiming superior quality control. On the other hand the Ministry of Petroleum and Chemicals imported the bulk product at a much lower rate and pointed out that it was equally good as the one sought to be especially imported by MSD.

Perhaps the government thought it was presenting MSD with a fait accompli, but MSD turned the tables on it by refusing to take the Ministry's bulk drug. At one time, the Chemical and pharmaceutical Corporation (CPC), a subsidiary of the State Trading Corporation, had reportedly more than Rs. 4 crores worth of the drug, with no takers. Unfortunately, there are no powers invested with Government to handle such situations, with the result that recalcitrant drug firms can refuse outright or drag their feet on drawing stock from the CPC whenever it suits their own purposes.

This sort of 'drug blackmail' resulted in alphamethyl dopa soon vanishing from the market, causing untold suffering to thousands of hypertensive patients in the country. Creating an artificial scarcity of such drugs is quite an established method of a making the government toe the line of the companies concerned. However, such brazen tricks are not played only by multinationals—even the Indian public

sector drug firms have allegedly indulged in them from time to time. And it is no coincidence that such a 'scarcity' usually develops in drugs that are essential (anti-TB drugs is yet another recent instance) and are usually not produced in enough quantitites by Indian firms. Whoever heard of a scarcity in tonics, vitamins and cough and cold 'remedies'?

The situation is only aggravated by the far from efficient working of the CPC, which is the only such canalising agency for bulk drug imports. There is reported to be a long time lag between the allocation and actual import of bulk drugs by the CPC, mainly because it has no regulation to carry over drug orders from previous years. Allocations are made every quarter of the year, but with typical bureaucratic functioning, things get delayed far too long. For instance, according to a recent report in the Financial Express the first quarterly allocation of the previous financial year was not made till last August. The only solution to this disorderly state of affairs in the CPC would be to have long-term contracts for essential drugs like methyl dopa, ampicillin, tetracyclines and anti-TB drugs, the report concluded.

Roche's Revenge

What happens to insignificant mortals who dare to rock the multinationals' boat (or rather, super-liner) has been brought out in stark details by a recent report in the New Statesman (march 7, 1980) written by Ms Ana Coote and titled, 'The Whistleblower's Reward'.

A few years ago, Stanley Adams, a senior executive with Switzerland's drug giant, Hoffeman La Roche, gave confidential documents to the anti-trust division of the EEC, that helped it indict Roche for unethi-cal practices. The documents proved the Roche had violated the Rome treaty, signed between Switzerland and the EEC, on two major counts: One, Roche had set up an illegal consortium with its chief competitors, with mutual agreements to adjust their output of vitamin products to certain fixed amounts, and two, that it had offered 'secret discounts' to clients that agreed to buy only from Roche. The EEC found Roche guilty on the second charge and fined it £160,000. And in may 1979 came confirmation of the penalty and rejection of Roche's appeal from the European Court.

Not surprisingly, Adams was soon forced into retirement by his employers, but that was only the beginning of a viciously vindictive campaign Roche launched against him. On New Year's Eve 1974, he was arrested on the Swiss border, and imprisoned for 'industrial espionage' under article 162 of the Swiss Penal Code and 'disclosure of secrets to the detriment of national security' under article 273, which Ms Coote stresses was designated to deal with foreign spies. How Roche's dirty deals tied in with Switzerland's 'national security' was not revealed. At any rate, in 1972, Switzerland and the EEC had signed an agreement to counter such 'drug abuse' by a 'firm in a dominant position' (a laughable euphemism for a colossus like Roche) but strangely enough, in cracking down

on Adams, Swiss courts superceded their own laws over the Swiss-EEC agreement.

Worse was to follow; Adam's wife was hounded by the Swiss police and committed suicide because they apparently led her to believe that her husband would be put behind bars for a very long time. She left notes saying 'she loved her children very much but could not face life' without him. After Adams was released on bail, he went to Italy where he had all along intended to establish a pig farm, with financial help from the Italian government. Things however had changed, and Adams found himself saddled with the unsavoury reputation of a common spy. His financial sources rapidly began drying up. As the campaign against him gathered momentum, and he slipped deeper and deeper into debt, L'Europa, an Italian paper, alleged that "a very senior Minister in the Italian government who was 'friendly with Roche' was masterminiding Adams' persecution. The allegation was not refuted, but the editor was promptly sacked. In depression Adams, who was once a Maltese citizen and had been a British consul once, applied for a British passport to emigrate to some other EEC country. But the then British Home Secretary refused to waive the usual five year residence clause. In December 1979, Adams was convicted of a very minor offence, and he wrote to his lawyer, "The court will come and empty my house of all my property and furnishings and belongings. Then my children will be out in the cold...."

On 21 January, 1980, the Legal Affairs Committee of the European Parliament, recognising the role Adams had played in punishing and stopping Roche's nefarious violations of the Swiss-EEC treaty, recommended that the Swiss government be asked to take amnesty measures for him and by paying him from the Community's budget, make good the loss he had suffered. A number of formalities have to be undergone before any such reparatory action can be taken. Meanwhile, Adam's plea, "For doing my duty, I find myself without work, without income, and with three children without a mother...." falls on deaf ears.

—Courtesy : *VHAI, New Delhi*

Selection of Appropriate Analgesic and anti-inflammatory Drugs

Dr. U. N. Jajoo

With advancement in pharmacology, more and more drugs are added to the list. A physician has choice to select a drug from a pool of drugs having similar therapeutic properties. Under the influence of persuasive selling practices of pharmaceutical firms, a physician tends to neglect the rationality and believes in the claims of drug industry, thus prescribes some costly drugs. The sufferer is the patient.

There are some guiding criteria which need to be followed by scientific minds before selecting a drug. Each drug needs to be weighed on the following criteria :

i) Effectivity or potency of the drug.
ii) Toxicity of the drug
iii) Cost
iv) Availability in the market.

An attempt is made here to rationally analyse analgesics and anti-inflammatory drugs on the above criteria.

Analgesics and anti-inflammatory Drugs

A few facts to note :

i) There is a large variation in the response of individuals to different analgesic-anti-inflammatory drugs, even when they are closely allied members of the same chemical family.

ii) If drugs must be given to a pregnant woman, low doses of aspirin are probably the safest.

iii) Only those drugs which are extensively tested by time should be used in children. This commonly means aspirin, indomethacin and ibuprofen.

iv) Most of the diseases where anti-inflammatory drugs are used,have a chronic course. This means palliative therapy with anti-inflammatory drugs needs to be continued for a long time. Thus, out of the above listed criteria toxicity and cost have priority consideration.

v) Fixed dose combination of different analgesics anti-inflammatory drugs must be denounced on the ground that their dose needs to be titrated in every individual and usually sensitivity of one drug cross reacts with others.

vi) Time-release preparations of salicylates are of limited value, since the half time for elimination is so long. Absorption from enteric coated tablets is some times incomplete.

viii) Salicylamide is no longer an official drug. Its effects in man are not reliable and its use is not recommened. The small doses included in "over the counter" analgesic and sedative mixtures are probably ineffective.

ix) Oxyphenylbutazone, a metabolite of phenylbutazone, has anti-rheumatic and sodium retaining activities similar to those of the parent drug. It is extensively bound to plasma-proteins and has a half life in plasma of several days. It accumulates significantly during chronic administration and contributes to the pharmacological and toxic effects of parent drug and hence ranks low as compared to phenylbutazone.

See Table No. 1 & 2

x) Acetamenophen has less overall toxicity and is thus usually preferred to phenacetin.

CONCLUSION :

Analgesic antipyretics :

i) Aspirin stands as the drug of choice, except in conditions where gastric erosion is endangered.

ii) For long-term use, aspirin stands as the drug of choice.

iii) Among injectable analgesics, there is little to choose. The cost is prohibitory for pentazocin and toxicity for analgin.

iv) For antipyretic effect-analgin remains the only significant injectable drug available in India (Injectable paracetamol has recently come into the market).

Anti-infalammatory drugs :

1. For chronic inflammatory joint disorders like osteo-arthritis, rheumatoid arthritis, ankylosing spondylitis-Aspirin remains the first drug of choice following Ibuprofen and Indomethacin.

2. For conditions like Gout, Indomethacin and phenylbutazone can be used keeping in mind their toxicity over prolonged use.

3. Aspirin remains the drug of choice in pregnant women and children.

4. Steroids score high in view of potency and low cost, but dangerous side-effects on long-term use necessitate it to be pushed down as a last resort. Their combination with non-steroid anti-inflammatory drugs may be denounced and are unethical.

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TABLE - I : Analgesics, - Antipyretics Selection of Appropriate Drug

Drug	Analgesic Efficacy & (Score–I)	Anti-Infl–ammatory Efficacy	Toxicity (Score-II)	Dose per Day	Cost of Treat-ment/day (Score-III)	Total Score (IxIIxIII)	Comments
Aspirin	++ (4)	0	(3)	1–2 gm.	300 mg. tab-2np. 14paise (5)	4x5x3= 60	
Paraceta–mol (Acetam–enophen)	+ (2)	0	(4)	1-1.5 gm	500 gm tab–15np 45paise (4)	2x4x4= 32	- Suitable substitute for aspirin in patie-nts when aspirin is contraindicated (peptic ulcer) or when the prolongation of bleeding time caused by aspirin would be a disadvantage. - A dose of 25 gm or more is potentially - fatal. Chronic abuse may cause methyamogl–obinaemia. - Drugs should not be used over a long time. Its combination in 'over the counter' drug is not justified. - If given should be a S. O. S. dose. - One of the common drugs incriminated in poisoning with analgesics in western world
Codein	+(2)	0	(3)	30mg QID	10mg. Tab-10 np.	2x3x1= 6	- Constipatory. Addiction potential less.
Dehydro– codein	++(4)	0	(3)	60mg QID	Rs. 1.80(1) Not available	-	
Dextropr- opoxyphen	++(4)	0	(4)	65mg QID	Available only in combination	-	- Minimal dependence.
INJECTABLE ANALGESICS							
Inj. Pent- azocin	++(4)	0	(4)	50–75mg QID	30mg/ml.- Rs. 2.5	–	- Small abuse potential (dependence).
Inj. Anal- gin	++(4)	0	(3)	500mg QID	500mg/ml-0.25 Rs.	–	- Standard pharmacological books does not mention this drug at all.

TABLE - 2 : Anti-flammatory drugs - Selection of Appropriate Drug

Drug	Analg-esic Efficacy	Anti-inflam-matory-Efficacy (Score-1)	Toxicity (Score - II)	Dose per Day	Cost of Treatment per day (Score-III)	Total Score (IxIIx III)	Comments
Aspirin	++	++++(4)	(4)	5 gm or more	300mg tab– 2np : 0 54p (5)	4x4x5-80	- Extensively used over long time. Safest drug in pregnancy.
Phenyl butazone	++	++++(4)	(3)	200-400mg.	200mg tab– 25np : 0.50Rs(5)	4x3x5–60	- Should not be given for more than 7 days due to cumulative toxicity - Cannot be used for chronic disorders for long time, not recommended in pregnancy. - Urico–suric drug.
Oxyphen butazone	++	++++(4)	(2)	200-400mg.	100mg tab- 25np : Rs1(4.5)	4x2x4.5 –36	- More toxic than the parent drug (Phe–nylbutazone).
Indomethacin	++	++++(4)	(2.5)	25–150mg/ day 75-100mg/ HS	25mg tab– 25np : Rs3.50	4x2.5x3 (3) 30	- High incidence of servere sdie effect over prolonged use - Not safe as Aspirin or buprofen – Urico–suric drug - Net recommened in pregnancy
Ibuprofen	++	++ (2)	(5)	600-1200mg	200mg tab– 60np : Rs.3.60(3)	2x5x3-30	– Better tolerated than other drugs
Naproxen	++	+++ (3)	(5)				- Not recommened in pregnant women or lactating mother.
Ketoprofen	++	+++ (3)	(5)	375-750mg	250mg tab- Rs.2 Rs.6 (1)		– cost prohibitory
Fenoprofen	++	+++ (3)	(5)				
Enfanamic acid	++	++ (2)	(5)	100-200mg.	Not available	–	
				300-600mg.	Not available		
Flufenamic acid	++	++ (2)		800mg Twice a day	400mg tab– 75np : kg. 3(3.5)		– Still under trial. An Indian product
Mefenamic acid	++	+ (1)		400-500mg	Not available		– More toxic, less effective
				750-1500mg	" "		- Not to be used for more than 7 days.
							– Safety during pregnancy is not established
Steroids (Prednisolone	0	+++++ (5)	(3)	5-7.5mg	5mg tab– 25np	5x3x5-75	– Drug of last resort in view of long term side effects.

COURTESY : VHAI – New Delhi

THE BANGLADESH BAN ON HAZARDOUS AND IRRATIONAL DRUGS
Its Review and the present Status

28th April 1982 :

An 8-member expert committee commissioned to evaluate all the pharmaceutical products in Bangladesh and draft a rational Drug Policy-met for the first time

Important outcome :

4140 products in the market were evaluated. 16 criteria were laid down for evaluation. (12 criteria selected on scientific grounds and 4 on politico-economic grounds).

Based on these, 1707 products were recommended to be banned. These were divided into 3 categories or Schedules as follows :

Schedule I - This included 265 locally manufactured and 40 imported drugs regarded as positively hazardous **to be banned immediately.**

Schedule II - included 134 drugs which required reformulation and were to be banned after a period of 6 months.

Schedule III - included **742 locally manufactured** and **526 imported** drugs. These drugs either had little or no proven therapeutic value or could easily be manufactured by local drug companies – instead of the multinatianals producing them at higher costs, there by depleting the country of much needed foreign exchange.

12th May 1982 :

The Expert Committee **submitted its report** to the Government.

29th May, 1982 :

The Chief Martial Law Administrator and his Council of Ministers **approved it.** The date of the ban of Schedule I was changed from 1 to 3 months and the banning dates of Schedule III drugs from 6 to 9 months.

7th June, 1982 :

Formal declaration of the new policy was made.

12th June, 1982 :

The Drug Control Ordinance was promulgated.

June, 1982 :

Reported pressure exerted on the Government by the Bangladesh American Ambassador on behalf of the US multinationa ls to have the policy amended. The negative stand of the USA regarding WHO's Intern ational Code against unethical marketing practices of milk food is well known.

The British, Dutch and the German Embassies joined to exert pressure on the government. The anti – gove rnment campaign having failed, the focus then turned to the Expert Committee which had recommended and pushed the drug policy.

July 1982 :

The 4-member Expert Scientific Committee of various pharmaceutical manufacturing companies was brought by the US Embassy to further pressurize thegovernment to **reconsider the ban.**

19th August, 1982 :

In Washington Post it was reported that the US State Department spokesman had acknowledged : "that the Pharmaceutical Manufacturers Association, a trade organization for the drug

industry, asked it to bring pressure on the Bangladesh government to delay implementing the law pending discussions with the manufacturers". He added : The State Department has a statutory responsibility for assisting American interests abroad. In this particular case, the US Government is also concerned that these regulations may inhibit further foreign investment in Bangladesh's US $ 30 billion market in the developing countries would be at stake if other countries followed suit.

12th August 1982 :

Report submitted by the Review Committe constituting of 6 military doctors set up to re-examine the matter in view of the pressure mounted by the multinationals and their respective governments.

6th September, 1982 :

The Drug (Control) Ordinance Amendment announced by the Government after studying the Review Committee's Report.

AMENDMENTS

SCHEDULE I :

Ban lifted from only 1 item of importance - Imodium (an anti-diarrhoeal).

Six other misused/abused dental remedies reinstated.

Total Ban of Schedule I Drugs will remain **Effective** 3 month period as decided earlier all harmful drugs to bedestroyed by 12th Septmber 1982.

SCHEDULE II :

4 eye preparations containing anti-biotic and steroid combinations allowed (contradictory to the Expert Committee's recommendation).

Heptuna plus a capsule containing iron, folic acid, multivitamins and minerals produced by Pfizer (very strangely) allowed to remain.

Ban withdrawn of total 7 drugs in Schedule II. Time limit extended according to the amended ordinance from 6th months to 12 months for the drugs listed in Schedule II.

Lobbying for this so called necessary ante-natal drug for the under-nourished anaemic pregnant woman was done by the country's gynaecologists headed by the President of Bangladesh Medical Association, shareholder and member of the Board of Directors of Pfizer, Begum Feroza.

Facts about the Bangladesh Drugs Scene in Brief :

-Bangladesh is the third poorest country in the world with a per capita income of US $ 70 a year.

-That 70% of annual drug sales are of drugs described as useless or therapeutically insignificant by the British National Formulary, the National Research Council, USA and the Federa Drug Administration, USA.

-Out of 51 products of Glaxo available in Bangladesh market in 1980, only 17 are available in the U. K. and only 1/3 are present in WHO's list of essential drugs.

-Of 31 products of Fisons available in Bangadesh, 17 were combination of vitamins and minerals. And only 5 of these drugs were available in the UK. 60% of Bangladesh's health budget is spent on drugs.

-In 1981 about 1250 million taka was spen on allopathic drugs in Bangladesh,

but due to poverty and the high cos of drugs less than 15% of the population was in a position to buy modern medicines.

SCHEDULE III

-28 drugs (manufactured under the third party licence) were allowed to remain. Time limit extended from 9 months to 18 months effective from 12th June 1982 – date of promulgation of drugs.

SCHEDULE IV (new)

Under this new schedule, 88 balms and vapours of small national companies were to be allowed to be manufactured for 18 months with effect from 12th June 1982.

WHAT'S NEW ?

All hazardous drugs of Schedule I were to be completely destroyed by **12th September 1982.**

There is a move on by the drug companies to apply for licence to export them to Saudi Arabia, Western Africa, etc, via Europe. These applications were made on 10th September with the support of Secretary of Health. The Drug Controller has refused and the matter has now been taken up with the Industrial Ministry. The Drug Controller has recommended that if this move should go through, all these productsshould be previously labelled saying the drugs was recommended to be destroyed in Bangladesh by 12th September 1982.

The failure of Sri Lanka and Pakistan to have a progressive drugpolicy has been quoted by the multinationals to subvert the attempts of Bangladesh Government to ban hazardous drugs.

What is probably the most humiliating comment on the social consciousness of Indian health personnel is that our drug policy is being quoted by the multinationals to criticize and condemn the Bangladesh ban. Hence it would not be out of place to quote from a medical journal from Bangladesh, 5th September 1982.

"In India, 43606 drugs are registered and sold. Even these have not upset their possibilities of further industrialization in spite of their technologocial advance and poverty....." (sic).

The above information is based on newspaper reports from Bangladesh and elsewhere and the personal communications from sociallyconcerned health personnel in Bangladesh like Dr. Zafrullah Chowdhury.

Availability of supply of essential life-saving drugs for the majority at easonreble cost, should come before profits of the drug companies. If these profits derive from the sale of haza rdous and irrational drugs or drugs with little therapeutic value, they need to be curtailed, and policies which allow drug companies to continue producing them need to be seriously questioned. We want a rational, people – oriented drug policy, and any effort in this direction anywhere has our support.

As mentioned in our handout "In Support of Bangladesh Ban" we repeat "Sabotage of this ban at this stage by the application of pressure or by money power will be a blow to all those who sincerely believe in socially relevant and socially just health care. Consequently, this is not a question of Bangladesh's fighting a 'Bangladesh problem'. It is in fact a question of a higher premium being placed on profits than on the welfare of human beings - if the ban is

withdrawn under duress. This is therefore a move against which the public opinion of all nations, particularly the developing countries should be raised. It is a cause worthy of global support specially from those involved in health-work'.

What would we do if we knew that the sale of hazardous and irrational drugs would continue because of the pressures and marketing strategies of the Drug companies ? Would we continue stocking them in our pharmacies and prescribing them ? We request our readers to boycott such hazardousproducts, because a Government ban on them may come too late, or never come because of vested interests.

If you are desirous of more information please write.

Mira Shiva

Co-ordinator,

Low Cost Drugs & Rational Therapeutics,

V. H. A. I., New Delhi

A STUDY ON PREVALENT DISEASES IN INDIA AND PRODUCTION OF SOME ESSENTIAL DRUGS

J. S. Majumdar L. N. Chakravorty Santanu Chatterjee

During 35 years after independence the pharmaceutical industry has shown rapid growth. The turnover of pharmaceutical formulations increased from Rs. 10 crores in 1948 to Rs. 1200 crores in 1981 1. But, the growth pattern of production dose not correspond with the disease pattern. The motive force of production of drugs was always the profitablity of the drug firms. The need of the suffering people was not considered while producing the drugs. This pattern of drug production continues till today. Hathi Committee gave its recommendations: New Drug Policy was announced in April, 1978; innumerable Committees were formed to give recommendations to the Central Government; but, the pattern of drug production did not change.

1. DISEASE PATTERN

Sixth five years plan (1980–85) took note of some prevalent diseases. The Planning Commission report states, " The diseases like TB, Gastro–intestinal infections, Malaria, Filaria, Infectious Hepatitis, Rabies and Hook worm are interrelated to environment. They accounted for 17.2% of morbidity and 20.8% of mortality in 1970 2."

The Planning commision report also states, that, "effective measures would be taken for balancing demand and supply of essential and life saving drugs. The pattern of drug production, import and distribution system would be rationalised towards the objective of promoting primary health care and to overcome the short supply of inexpensive anti-infective drugs like sulfonomides, anti–T. B. drugs anti–leprosy drugs like dapsone etc 3."

However, the study of production pattern during last few years does not reveal that the Government's administrative machinery was serious to implement the decisions nor the industry has taken the Planning Commision report seriously. Like most of the programmes, these also remained only on paper.

WHO identified six tropical parasitic diseases as prime targets for major efforts in the developing countries including India. Amongst these are Filariasis, Malaria and Leprosy. UNIDO reported that the major health problems of the developing countries in South East region are Malaria, Diarrhoeal diseases, Tuberculosis and Leprosy 4.

In our country, from various available reports, it is well established that the major diseases are Filaria, Tuberculosis, Malaria, Leprosy, Enteric Fever, Dysentery, Gastro–enteritis etc. It is estimated that there are about 18 million people suffering from filarial parasitic stage while 14 million persons are suffering from irreversible disease manifestation like Elephantiasis 5. It is further estimated that nearly 10 million patients are suffering from active Tuberculosis of lungs 6. However, amongst them only 6.12 lakhs persons were brought under treatment in 1980 (Figu–

Paper presented in the Drug Workshop, organized by the Voluntary Health Association of India, Jaipur, 30 & 31 August, 1982

res from Assam, Bihar, West Bengal, J. & K., Manipur and Nagaland were not available and therefore not included) 7, From this it will be evident that vast number of T. B. patients do not get adequate treatment and supply of modern medicines. The following table will show the magnitude of the problem.

NUMBER (Estimated) OF PERSONS SUFFERING FROM THESE DISEASES IN 1980

Diseases	No of Persons
Filaria (Parasitic stage)	18 million
T B. (Active Pulmonary)	10 million
Malaria	2.84 million
Leprosy	3.3 million
* Enteric Fever	0.3 million
* Dysentery	5.7 million
* Gastro-enteritis	7.8 million

(* Assam, Bihar, West Bengal, J. & K., Manipur and Nagaland where not included).

Source : Health Statistics of India, 1981, Ministry of Health and Family Welfare : Rajya Sabha proceedings September, 1981.

The majority of the patients do neither get the treatment nor supply of the medicines. Only a small number of patients are supplied with modern medicines.

2. ESSENTIAL DRUGS FOR THE TREATMENT OF THESE DISEASES

UNIDO in its report of November 21. 1980 enlisted the following essential drugs in the developing countries for the treatment of these diseases.

i). Chloroquin
ii). Metronidazole
Iii). Chloramphenicol
iv). Dapsone
v) I. N H.
vi). Ethambutol
vii). Streptomycin
vii) Diethyl Carbamazine Citrate
ix). Piperazine

In our country the following drugs have been recommended as essentail drugs for the treatment of the prevalent diseases 8.

Malaria	-	Chloroquin
Dysentery	-	Halogenated Quinoline Metronidazole
Enteric Fever	-	Chloramphenicol and its esters
Leprosy	-	D. D. S. and derivatives
T. B.	-	Streptomycin, I. N. H., PAS and its salts, Thiacetazone, Ethambutol
Filaria	-	D. E. C. Citrate
Worm Infestation	-	Piperazine and its salts

3. PRODUCTION TREND OF ESSENTIAL DRUGS :

The production of these essential drugs for the treatment of prevalent diseases in the country have suffered due to the manipulations by the drug manufacturers and total negligence on the part of the administration. While essential and life saving drugs have been deliberately kept under low production, the drug industry has emphasised more on the non-essential drugs. The population of third world countries, who are suffering from these tropical parasitic diseases, were compelled by the industry to purchase vitamins and tonics in abundant quantity. The sale of vitamins and tonics in third world countries, percentage-wise, are higher even from the developed countries, The following figures will reveal the fact.

AVERAGE SHARE OF CONSUMPTION OF VITAMINS & TONICS 9 AT RETAIL LEVEL, 1975-77

Percentage range of market share

Developed contries :	Developing countries :
3.0 – 8.0	5.0 – 12.0

That means, whatever percapita expenditure is there on drugs, the patients in India are made to pay more for the vitamins and tonics than the industrialised developed countries.

While the industry is producing vitamins, tonics, nutritive supplements and such other products which give them increased profits, much beyond the licenced capacity ; there is a deliberate attempt to cut the production of essential drugs under the plea of less profit. Neither the industry cares for the treatment of the millions of people suffering from dreaded diseases nor the Government administration is concerned for the medical need of these patients.

The following figures will show that not only the production of these essential drugs are much below the licenced capacity, the production is actually even below the actual consumption which is far below the actual need.

CONSUMPITION, INSTALLED CAPACITY AND PRODUCTION OF SOME ESSENTIAL DRUGS IN 1978.

Drugs	Accounting Unit	Installed Capacity	Consumption	Actual Production
Streptomycin	Tonnes	257	296.86	240 (DGTD)
Chloroquin	Tonnes	176	346.51	45
I N H	Tonnes	539	105.54	95.6 (DGTD)
Dapsone	Tonnes	38	24.76	17
D. E. C. Citrate	Tonnes	56	24.25	23
Piperazine	Tonnes	165	194.33	74

(Source : 1. For Installed capacity and actual production – Indian pharmac–eutical Guide, 1980.

2. For actual consumption - Indian Drug Statistics, Ministry of Petroleum, Chemicals, Fertilizers, Govt. of India, 1979–80

3. Actual production of Streptomycin and INH have been taken from DGTD annual report, 1978–79)

Out of these total productions, Public sector produced in 1978–79 a substantial quantity which will be revealed from the following figures :

DRUG	UNIT	QUANTITY
Piperazine	IDPL	72–80 T.
Streptomycin	IDPL	36.30 T.
	HAL (77–78)	87.00 T. *

(Source : Statement of Minister in Rajya Subha on 22.3.82 * and Indian Pharmaceutical Guide, 1982.)

The following figures will further establish the fact that the DGTD units, which is commonly know as organised sector, always produced these drugs much below their installed capacity.

Continued overleaf

PRODUCTION OF ESSENTIAL DRUGS

(BY DGTD Units only)

Products	Accounting Unit	1976		1977		1978	
		Installed Capacity	Production	Installed Capacity	Production	Installed Capacity	Production
Streptomycin	TONNES	257	224	337	208.9	337	240.8
Chloramphenicol	-do-	128.8	93	129.8	90.6	129.8	82.5
Halogenated quinolin	-do-	490.6	190	474.4	143.66	474.4	200.8
D. D. S. and its derivatives	-do-	23.3	18	25.8	16.3	25.8	15.9
I N H	-do-	374.56	98	473.56	56.5	473.56	95.6
PAS and its salts	-do-	1170	695	1350	564.70	1350	552.21
Thiacetazone	-do-	152.6	14	142.56	22937 Kg	142.56	12470 kg
Quinine and its salts	-do-	-	17	-	15.9	-	25.8
Diethyl C. C.	-do-	56	11	56	18.69	56	22.1
Piperazine and its salts	-do-	-	118	-	108.9	-	55.3

(Source : DCTD Annual Report 1978-79)

In reply to a question in Lok Sabha on December 15, 1981 Shri Dalbir Singh, the Minister of State for Petrolium, Chemicals and Fertilizers, admitted that essential and life saving drugs like Chloramphenicol, PAS and its salts, INH, Iodochlorhydroxy-quinoline, Piperazine Hexahydrate, Dapsone, D. E. C. citrate etc. have shown declining trend in production, The following figures will establish the trend.

ACTUAL PRODUCTION

Drugs	1980 (April to September)	1981 (April to September)
Chloramphenicol	46.41 T.	36.16 T.
PAS and its salts	215.16 T.	122.22 T.
I N H	69.18 T.	53.70 T.
Idochlo - Hydroxy - Quinoline	77.65 T.	47.73 T.
Piperazine Hexahydrate	6.30 T.	4.20 T.
Dapsone	10.27 T.	10.17 T.
D. E. C. citrate	10.58 T.	8.42 T.

The country has sufficient indigenous technical know how for the production of these life saving and essential drugs. Instead of encouraging indigenous production and instead of compelling the industry for full capacity utilisation in the production of these drugs, the Govt. is relying more and more on import of these drugs. The following figures will establish this fact.

IMPORT OF ESSENTIAL AND LIFE - SAVING DRUGS WHICH ARE ALSO INDIGENOUSLY PRODUCED DURING 1980 - 81.

Products	Unit	Estimated Production	Quantity imported	Value Rs. in lakhs.
Streptomycin	Tonnes	238	44.1	123.69
Chloramphenicol	-do-	108	165	570.38
Chloroquin	-do-	34.9	71.8	161.26
Piperazine	-do-	86.7	25	4.65
Dapsone	-do-	22	33	4.96

(Source : Production Figure (Estimates) :
Ministry of Petroleum, Chemicals, Fertilizers.
Imports : Data complied by DGHS
Quoted in : OPPI Bulletin. Nov - Dec. 1981,)

While most of the drug manufacturers have applied for the regularisation of excess production beyond the licenced capacity in response to the Central Government's Industrial Policy Statement and the Petro-chemical Ministry's liberalised stand in this regard, no attention has been given for full capacity utilisation of the production of life saving and essential drugs. In the following few paragraphs attempts have been made to analyse the situation with particular reference to the treatment of Tuberculosis and production of Chloramphenicol.

4. DETAIL STUDY OF PRODUCTION OF ANTI-TB DRUGS

On 20th April, 1982 Sri Dalbir Singh, the Minister of State for Petroleum, Chemicals and Fertilizers, made a statement in Lok Sabha that PAS and its salts and INH production were showing declining trend during April 1981 to February, 1982 He further stated, "the decline in production is due to (1) demand constraints or shifts, (2) Industrial unrest, (3) Availability of cheaper imporugs."

From the available data and facts it will be revealed that the Minister was either wrongly informed or was giving wrong information.

There is no demand constraints or shifts as far as anti - TB drugs like INH and PAS are concerned. It was earlier stated that out of estimated 10 million patients suffering from active tuberculosis of lungs over 6 lakhs patients (except a few States) were reported under treatment. Vast number of other patients have no access to modern medicaments. The talk of demand constraints or shifts is only to hide this fact. The projected requirements during the sixth five year plan does not show that there is a declining demand of INH & PAS as reported by the Minister.

Actual Production and Requirements of Anti-TB Drugs in Tonnes

Nome of the Product	Actual Production 77-78	Requirements 78-79 Base year	82 83	83-84
P N H	79	175	375	450
I A S	548	750	1300	1500
Thiacetazone	26	35	60	70
Ethambutol	3	20	90	110
Rifampicin	Nil	3	6	7

The compound rate of growth, during this period, of INH is 20%, PAS and Thiacetazone 15%, Ethambutol 22% and and Rifampicin 16%.

(Source : Report of the "Working Group on the Drugs and Pharmaceutical Industry for the plan period (1978-79 to 1983-84)", Government of India, Ministry of Petroleum Chemicals and Fertilizer (Department of Chemicals and Fertilizer)

Streptomycin, INH, PAS and Thiacetazone are well established anti-TB drugs. The auto-toxicity of Streptomycin has been accepted as a hazard of the treatment and sufficient care is being

taken. Similarly, Thiacetazone is also recommended with caution. But, the fact remains that indigenous technology is available for the production of these drugs and the country can be fully self reliant with proper planning. Resistance to these drugs are rarely reported when properly used in combinations. Therefore, there cannot be any demand constraints for these reasons nor there are demand shifts. It is well established now that poverty, malnutrition and absence of proper hygiene prepares the ground for invasion of tuberculosis. Most of the T. B. patients cannot purchase medicines of their own. If any demand constraints is there, it is due to the price factor and that to not the total expenditure but per day expenses on drugs. Therefore, there cannot be shift in general towards Rifampicin and Ethambutol.

Further, Rifampicin is not indigenously produced. The drug is totally imported. The import of this drug was

1979-80	1980-81	1981-82
5413.5 kg	8948.5kg	15785.5 kg

Such a small quantity of imports can hardly meet the actual needs of the T. B. patients. In addition, Rifampicin is also used for the treatment of Leprosy in combination with Dapsone. The drug is costly. The CIF cost per unit during 1981-82 was Rs. 4130/- per kg. The technology of manufacturing of Rifampicin is only known to two companies in the world – one is in Italy the other is in Switzerland. They are having the monopoly over manufacturing this drug. The donor of Rifampicin in India is Swedish International Development Agency (SIDA). (10)

It will be evident from these facts that demand can hardly be shifted towards Rifampicin, which is costly, wholely imported and technological know-how is not available in India.

As far as Ethambutol is concerned, the actual production in the country from imported intermediaries during 1979-80 was 23.53 tonnes. In addition 96.19 tonnes were imported during this period.

From this, it will be evident that more emphasis is given for the import of the drug than the actual production.

On one side deliberate attempts were made for creating shortages of INH & PAS by cutting down the indigenous production, on the other side import of costly drugs are encouraged on the plea of demand shifts. Instead of natural demand shift, attempts have been made to deliberately create a condition to make room for costly and imported drugs, and for this millions of poor T. B. patients have to pay the price.

The production pattern of Pfizer Ltd. is a classical example of under-production of essential anti-T. B. drugs and over-production of non-essential products.

Products	Licensed capacity	Production 1978	Production 1979
INH	80 Tonnes	45 Tonnes	52 Tonnes
PAS and its salts	110 "	90 "	94 "
Protienex	110 "	269 "	290 "

(Source : From Company reports)

In their attempt for deliberate cut in the production, the industry and the Government take different plea including so-called labour unrest. In reply to a question in Lok Sabha on 18th August, 1981, the Minister of State for Petroleum, Chemicals and Fertilizers, stated, "Periodical shortages of PAS granules manufactured by M/S Pfizer Ltd. were reported from Delhi in the recent past. The matter was taken up with the manufacturers who reported that as they had closed down for some time due to labour unrest and later were affected by go slow, their production and supplies of the above formulation was affected."

Whereas, the factory manager of M/S Pfizer Ltd. issued a notice on 26th March, 1981 which reads, :

"TO EMPLOYEES OF PAS SECTION :

"It is hereby notified for the information of Employees of PAS section that due to the sudden steep increase in the price of MAP without a corresponding increase in the price of the finished product, it has become uneconomical to produce PAS and, therefore, it has become necessary to suspend operations in the PAS sections of chemical plant. We are making all efforts to secure a price revision of the finished product.

Employees of PAS section will be temporarily transferred to other departments with effect from April 6, 1981, to date from which PAS operations will be suspended."

THANE, DATED MARCH 26, 1981

for Pfizer Limited
Sd/- B. B. Roy
Factory Manager"

From the above statements it would be evident that attempts were made by the company to hide the fact that they stopped production of PAS granules as the profit margin was less compared to products like Protien Hydrolysates Tetracyclines, vitamins etc. They wanted to take the plea of "Labour Unrest".

The Government did not care to investigate the facts and simply passed on the false information given by the company.

In reply to another question in Lok Sabha on 18th August, 1981, the Minster informed that though Pfizer's PAS granules were in short supply, the equivalent brand of PAS granules (Biological Evans) was available. A study in the market revealed that PAS granules of Biological Evans was not available since December, 1980. The company stopped supplying PAS granules to the since January, 1981. This is only an trade example to show in what manner Government machinery functions to find out the facts in respect of supply of essential drugs.

By a confidential circular of May 26, 1981, Pfizer Ltd. informed their Regional Managers that they could quote special hospital price for their tetracycline and some other group of products in a special rate less than the usual trade price. But, the circular states, "the availability of narrow spectrum injectables and Anti-TB dosage forms will be very uncertain". This conclusively proves that there was no demand shift from INH and PAS but an artificial shortage was created for these drugs.

A survey in the market also revealed that PAS of Pfizer and Biological Evans are not available since early 1981.

Similarly, Streptomycin of Pfizer and Glaxo are not available for many years. INH is also in short supply periodically.

The above facts will prove that there was neither a demand shift nor labour unrest due to which these essential Anti-T. B. drugs are not avilable in the market and there is a declining trend in the production.

5. STUDY ON CHLORAMPHENICOL PRODUCTION :

Not only indigenous production of Anti-TB drugs are being replaced by drugs against the interests of the patients, similar attempts are being made in respect of Chloramphenicol also.

Three companies are the major manufacturers of Chloramphenicol in India. Parke-Davis with a licensed capacity of 20 tonnes manufactures Chloramphenicol starting with P-Nitro-acetophenon. Boehringer Knoll with 60 tonnes of capacity manufactures Chloramphiencol from Benzyldehyde. For the production of Chloramphenicol from these intermediaries 32% foreign exchange is required. Dey-Se-Chem has the technological know-how for production of Chloramphenicol from basic stage making it almost self-sufficient for indigenous production with only 5% foreign exchange requirements. It has 60 tonnes of licensed capacity. But, the company did not produce Chloramphenicol from the basic stage since inception in 1972 except few kgs. in 1977 and 1978. Some Chloramphenicol was produced by Dey-Se-Chem from imported L-Base, the penultimate. This also has been stopped completely from early 1981.

It was admitted in the Lok Sabha by the Minister of State for Petroleum, Chemicals and Fertilisers,

"Some instances of sale of Chloramphenicol at prices lower than the Government fixed pool prices have come to the notice of my Ministry. Some parties who are importing the penultimate intermediate L-Base are converting it into Chloramphenicol and are selling the same at lower prices". 12

It is not some instances. In fact the entire Chloramphenicol production today in the country is from L-Base, the penultimate, for one stage conversion involving 84% foreign exchange. The country has the technological know-how for indigenous production of Chloramphenicol. But, due to the wrong policy pursued by the Government, the factories, for Chloramphenicol production from basic stage and from Formaldehyde route, are kept idle. L-Base is allowed to be imported in large quantity. Further 165 tonnes of Chloramphenicol powder were imported straightway.

From the study of the production pattern of anti-TB drugs and Chloramphenicol it may be concluded that artificial shortages are being created of essential and life saving drugs which are required for the treatment of prevalent diseases in this country. Instead of encouraging indigenous production emphasis is more shifted for the imports of drugs either in finished forms or the penultimates.

The policy statement of drugs aims at, "the development of self reliance in drug technology" making drugs available at reasonable prices and in abundance to meet the health needs of the people" (13) etc The aims are totally defeated by the wrong drug policy pursued by the administration and by the industry.

6. SALES PROMOTION PATTERN

Though the expense ratio on R & D. in pharmaceutical industry is little over 1% of the total turnover compared to more than 10% in developed countries, the promotional expenses in India is at par if not more compared to many developed countries (14).

India	-	18%
Sweden	-	18%
France	-	17%
U. K.	-	15%

The following were the leading pharmaceutical companies on global basis in 1974. (15) Roche, Merck, Hoechst, Ciba Giegy, Bayer, Sandoz, American Home Products, Pfizer' Warner, Abbott, Boehringer, Squibb, Glaxo, Searle, cyanamid, S. K. & F, Johnson & Johnson I. C. I.

These companies are also marketing their products in India. American Home Products has its subsidiaries in Wyeth Group of companies. Squibb products are marketed by Sarabhai Chemicals.

The sales promotion pattern of these companies will show that these multi–antionals do not promote the essential and life saving drugs for the treatment of T. B , Leprosy, Filaria, Malaria, Enteric Fever, Dysentery, Gastroentoritis. etc.

PROMOTION OF DRUGS BY THE MULTINATIONAL AND ORGANISED SECTOR (16)

June 1981 to June 1982

Companies		Drugs Promoted
1. Roche	-	Co-trimoxazole, Multivitamin, Diazepam, B-Complex
2. E. Merck	-	Vitamin E ; B/1 B/6 B/12 combinations
3. Ciba–Giegy	-	Anti Depresant, Progesterone - Oestrogen Combination ; Nasal Drops : Sulpha Drugs
4. Pfizer	-	Tetracyclines ; B – Complex ; Protien Hydrolysate
5. Warner	-	Anti asthmatic ; Antacid ; Iron Tonic
6. S. K. & F.	-	Iron Capsule ; Iron–Vitamin Combination and Tonic
7. Parke – Davis	-	Malt preparation, Cough expectorant, Enzyme and Multivitamin Drops.
8. Glaxo	-	Steroid ; Calcium Syrup ; B/1, B/6, B/12 Combination ; Cough Syrup ; B–Complex ; Vitamin–Minerals Combination.
9. Sarabhai	–	Doxycycline and Amoxycillin of Fleming Pharmaceuticals (small scale sector) ; Cough Syrup, Nutritional Supplements.
10. Burroughs Wellcome	-	Contrimoxazole ; Tropical Antibitotic ; Analgesics, Anti histamines
11. Cyanamid	:	Teracycline ; Ethambutol ; B–Complex Iron Capsule ; Multivitamin

12. Abbott - B–Complex ; Multvitamin ; Erythromycin
13. ACCI (ICI) – Anti hypertensive ; Anti hyperlipids
14. John Wyeth – Steroid ; Antacid ; Analgesic Anti Histamines

From the above it will be observed that entire sales promotion efforts were to sell Vitamins, Tonics, Nutritional supplements, Cough Syrups, Analgesics Enzymes etc. These Companies did not try to promote any drug for the treat–ment of prevalent disesaes as already mentioned.

These companies, though have the lions share in the medicine market they did not contribute much in the treat-ment of prevalent diseases as will be evident from the following statement :

Production of Essential Drugs by Multinationals and organised Sector(17)

Name of the firms	Anti T B					
	INH	PAS	THIACETAZONE	ETHAMBUTOL	RIFAMPICIN	STREPTOMYCIN
Abbott	Nil	Nil	Nil	Nil	Nil	Nil
ACCI	Nil	Nil	Nil	Nil	Nil	Nil
Hoechst	Nil	Nil	Nil	Nil	Nil	Nil
S. K. & F.	Nil	Nil	Nil	Nil	Nil	Nil
Searle	Nil	Nil	Nil	Nil	Nil	Nil
Sandoz	Nil	Nil	Nil	Nil	Nil	Nil
Roche	Nil	Nil	Nil	Nil	Nil	Nil
Parke-Davis	Nil	Nil	Nil	Nil	Nil	Nil
Sarabhai	Yes	Nil	Yes	Yes	Nil	Yes
Beohringer Knoll	Nil	Nil	Nil	Nil	Nil	Nil
Glaxo	Nil	Nil	Nil	Nil	Nil	Yes
E. Merck	Nil	Nil	Nil	Nil	Nil	Nil
Ciba-Giegy	Nil	Nil	Nil	Nil	Nil	Nil
Pfizer	Yes	Yes	Yes	Nil	Nil	Yes
Warner	Yes	Nil	Nil	Nil	Nil	Nil
Burroughs Wellcome	Nil	Nil	Nil	Nil	Nil	Nil
German Remedies	Nil	Nil	Nil	Nil	Nil	Nil
CYNAMID	Nil	Nil	Nil	Yes	Nil	Nil
Ethnor	Nil	Nil	Nil	Nil	Nil	Nil

Production of Essential Drugs by Multinationals and Erganised Sector (17) (contd)

Name of the firms	INH	PAS	THIACETAZONE	ETHAMBUTOL	RIFAMPICIN	STREPTOMYCIN
John Wyeth	Nil	Nil	Nil	Nil	Nil	Nil
	Anti-worm piperazine	Anti-Leprosy Dapsone	Anti-Malaria (Chloroquine & derivative)	Anti-Filaria D.E.C. Citrate	Anti-Enteric Chlorophenicol	Anti-Amoebic Quinoline, Metronidazole and similar preparation
Abbott	Nil	Nil	Nil	Nil	Nil	Nil
ACCI	Nil	Nil	Nil	Nil	Nil	Nil
Hoechst	Nil	Nil	Yes	Nil	Yes	Nil
S. K. & F.	Nil	Nil	Nil	Nil	Nil	Nil
Searle	Nil	Nil	Nil	Nil	Nil	Yes
Sarabhai	Nil	Nil	Nil	Nil	Yes	Nil
Sandoz	Nil	Nil	Nil	Nil	Nil	Yes
Roche	Nil	Nil	Nil	Nil	Nil	Yes
Parke – Davis	Yes	Nil	Yes	Nil	Yes	Nil
Boehringer Knoll	Nil	Nil	Nil	Nil	Yes	Nil
Glaxo	Yes	Nil	Nil	Nil	Nil	Nil
E. Merck	Nil	Nil	Nil	Nil	Nil	Nil
Ciba - Giegy	Nil	Nil	Nil	Nil	Nil	Yes

THE HARMFUL FOOD — DRUG COMBINATIONS

Mary was suffering from a compulsive eating disorder for which her doctor had prescribed the anti-depressant, Nardil, (phenelazine sulphate) one of several useful drugs known as MAO inhibitors. Unfortunately, Mary's doctor, not wanting to upset her, failed to warn adequately of the serious danger of eating certain foods while on the drug. One day Mary went on a binge that included chocolate and cheese, and she died.

While the extreme outcome of Mary's case is unusual, untold thousands suffer adverse reactions each year because they consume hazardous mixtures of drugs and food or drink. Thousands of others lose the full benefit of the drugs they take because they consume food or drink that inactivates the medication or slows its absorption.

Still others needlessly experience gastrointestinal upset from drugs precisely because they fail to take the medication with food. Finally, some people who use medications on a chronic basis may develop nutrient deficiencies as a result of drug-food interactions; special dietary supplements may be needed to compensate.

There are so many drugs and so many safety rules for taking them — with new drugs and new rules being discovered all the time—that doctors are hard put to keep up with and remember them all. The busy physician with a prescription pad in hand is not likely to look up the advice for every drug and give appropriate warnings to all patients.

Many pharmacies now label prescriptions with instructions on how to take them, but this is neither a universal practice nor necessarily an adequate solution. Besides, some of the worst offenders in drug-food combinations involve over-the-counter medications.

It is important for the patient to ask the doctor or pharmacist how each drug should be taken and what, if anything, to avoid while taking it. "Take on an empty stomach" is not an adequate instruction, since you may think that means to take it just before eating; actually it means two to three hours after your last meal and at least an hour before the next one to give your body a chance to absorb the drug without interference from food.

The precautions described below can help to assure that the drugs you take will not make you sicker and will help you in the way they are supposed to.

Harmful combinations: MAO inhibitors – Nardil, Marplan (Isocarboxazid), Eutonyl, Parnate, (Tranyl cypromine) Niamid, (Nialamide) Matulane, Fuoxone and Eutron. These are used to counter depression and sometimes to lower blood pressure and treat infections and cancer. When foods containing the substance tyramine are eaten while on such a drug, blood pressure can soar and precipitate a hemorrhagic stroke and death. Less severe reactions can warn of danger ahead; they include bad headaches, sweating, rapid pulse and vision changes. The foods to avoid include aged cheese, aged meat and sausage, chicken liver, fava beans, pickled herring, anchovies, avocados, Chianti wine, Sherry, chocolate, sour cream and yogurt.

Anticoagulants—Coumadin, Dicumarol Bishydroxy coumarin, Liquamar, Panwarfin (Warfarin Sodium), Sintrom, Miradon and heparin. These are given to thin the blood and stave off clots. You should avoid excessive consumption of foods rich in vitamin K, which promotes clotting. Among them are leafy greens, asparagus, bacon, broccoli, brussels sprouts and beef liver, Anticoagulants may also conflict with garlic and onions (two ounces or more), according to a pharmacist and author of an excellent consumer's guide to safe and sensible use of medications.

Thyroid hormonea — Thiouracil, Euthroid, Choloxin, Synthroid, Thyrolar, Proloid, Cytomel. Certain foods — brussels sprouts, cabbage, cauliflower, kale, mustard greens, rutabaga, soybeans and turnips—contain "goitrogens" that interfere with thyroid hormone and may lead to goiter.

Aspirin & antibiotics

Antibiotics — Including numerous brands of erythromycin, penicillin, tetracycline and griseofulvin. Erythromycin, penicillin and ampicillin are partly destroyed in the stomach when consumed with acidic foods, such as citrus fruits, tomatoes, fruit juices and drinks, colas, wine, pickles, vinegar and caffeine. This can result in a less than effective dose, slowing recovery and possibly allowing drug-resistant infectious organisms to develop. Tetracycline combines with the calcium in milk, dairy products and sardines, rendering it less effective. Griseofulvin, an antifungal drug, is absorbed best when you eat fatty foods (taking the drug with a teaspoon of vegetable oil can help) and least well absorbed on a high-protein diet.

Aspirin and aspirin combinations—when consumed with acidic foods (see antibiotics) and alcoholic drinks, aspirin's irritating effects on the stomach are intensified and may result in ulcers or serious gastric bleeding.

Diuretics—Aldactone, Aldomet, Spironolactone Alphamethyldopa, Aquatag, Diurel, Esidrix, hydrochlorothiazide, hydrodiuril, Lasix, (Furosemide), Oretic, Unipres, among other drugs that remove excess water from the body. When consumed with foods rich in monosodium glutamate (MSG), such as many Oriental dishes, or containing seasoned salt and meat tenderiser, water loss can be dangerously enhanced. In addition, imported licorice candy and flavouring, which can counter the benefits of diuretics and deplete the body of essential potassium,

TAKING MEDICATIONS

On an empty stomach

(At least one hour before or two hours after meals)

Ampicillin, amoxicillin, cloxacillin (Tegopen), erythromycin, isoniazid, levodopa, lincomycin, methacycline, oxytetracycline, penicillamine, penicillin G. Pencillin V. Prostaphlin, rifampin, tetracycline (except declomycin), Unipen.

Half-hour before meals

Belladonna and derivatives, Donnatal, Librax, Preludin, Pro-banthine, Pyridium, Ritalin.

With meals or food

Aminophylline, antidiabetics, APC, Artane, chlorothiazide (Diuril and Hydrodiuril), Darvon Compound, Dilantin, Dyrenium, Flagyl, griseofulvin, Hydralazine, Inderal, Lithium citrate, Lopressor, nitrofuration (Furadantin and Macrodantin), pediamycin, phenylbutazone, Ponstel, prednisolone, prednisone, propoxyphene, propranolol, rauwolfia and derivatives, reserpine, Ser-ap-es, Temaril, Unipres, Vibramycin (doxycycline).

Without milk

Dulcolax, potassium chloride, potassium iodide, tetracyclines (except doxycycline).

Without fruit juices

Ampicillin, benzathine penicillin G. cloxacillin, erthromycin.

should be avoided. Those regularly taking diuretics should increase consumption of foods rich in potassium, such as oranges, bananas, cantaloupe, dried fruits and peanut butter.

Antihypertensives—The diuretics plus reserpine, Eutronyl, Eutron, Sandril, (Propranolol) Inderal and other drugs that lower blood pressure. Avoid natural licorice (see diuretics), which can lead to salt and water retention and potassium loss, resulting in a dangerous increase in blood pressure.

Phenacetin and theophylline—Studies show that phenacetin, a painkiller in many over-the-counter and some prescription drugs, can be partly inactivated by brussels sprouts and cabbage. Phenacetin and the asthma drug theophylline may also be blocked by charcoal-broiled foods.

For the most part drugs and alcohol do not mix. Alcohol can react, to your detriment, with more than 100 drugs. The rule of thumb should be: If you're taking medication, don't drink unless you have been given explicit approval by your physician.

Alcohol aggravates the side effects of aspirin and aspirin combinations and Paracetamol — (Crocin, Tylenol, Datril, etc.) It can raise blood sugar and thus interfere with the activity of diabetes medications. **— New York Times.**

Courtesy: *The Hindu, Oct. 24, 1982*

Guidelines for Submission of Manuscripts

The Editor requests contributors of articles to kindly submit TWO copies of the manuscripts typewritten and double spaced. Full names of all Authors with their academic and administrative positions may please be provided.

Thank you

THE GREAT HEALTH ROBBERY

The theme of the discussions at the eighth General Body Meeting of VHAI held in Ahmedabad in April 1982 was "The Great Health Robbery".

The participants identified four groups of people who were deprived of their right to good health viz., children, women, people who need medicines and workers. They made some positive suggestions for action to be taken at the individual, the State and the National levels.

VHAI will be grateful for your attention to these valuable suggestions. Your collaboration in drawing up an action plan is indispensable.

At the individual level

Children

Children are sensitive and perceptive; therefore, we must practise what we preach.

Women

a. Through introspection and meditation, women must become aware of the full potential of their own strength and spiritual power.
b. Women must go in for vocational skills and education and try to be economically self reliant.

People who need medicine

a. As an individual to respond sensitively to the need of another for medicine in as many ways as our personal resources make it possible.
b. The organisation of an area-wise information service to keep upto date information on location or availability of scarce life-saving medicines.

Workers

a. Workers should be recognised as individuals capable of making decisions for themselves.
b. Protect workers in our individual institutious against occupational hazards.
c. Provide them with the facility to redress grievances.

At the State Level

Children

a. Adopt, adapt and carry out NANI plans vigorously.
b. Increase programmes for mother education in nutrition.
c. Projects to increase family incomes, so they could have more energy rich foods.
d. Education of doctors about the needs of children with protein calorie malnutrition.
e. Promote education on the value of jaggery, against refined sugar, as better food.

Women

a. Organisations must provide self-employment schemes for women; greater economic freedom will bring women greater social freedom.
b. Compulsory Primary Female Education, its strict implementation is important to raise the status of women.
c. Since enhancing women's income improves her health, even part time employment can begin the process of helping her become more free. Society must make this possible.
d. Concerted drives and campaigns by voluntary organisations against social evils like dowry, obscene advertising and films denigrating the image of women, job and wage discriminations etc. must be encouraged.
e. The establishment of co-operatives or trade unions of working women would help.

People who need medicine

a. To help purchase bulk medicines at regional and State levels; where possible from the government for the national eradication programmes.
b. To provide ways and means to deal with the problems of spurious drugs by
   i. developing laboratory facilities where needed

ii. improving the excisting facilities
iii. involving voluntary groups in the detection of spurious and adulterated food drugs.

c. Promote appropriate health and use of drugs through seminars, literature, etc.

d. Demand Code of conduct of marketing for the pharmaceutical industry.

e. Demand more facilities for research and practise of indigeneous systems.

f. Build up public opinion for shifting the licensing and pricing of drugs from petroleum to Health Ministry.

Workers

a. To press for the implementation of the minimum wages legislation so that the worker is able to otain the required volume of calorie prescribed by the ICMR Study.

b. Creation of workers recreational outlets to minimize recourse to alcoholism.

c. Press for the provision of adequately equipped cafetaria to provide variety and nutritious foods to workers on a co-operative basis.

d. Establish stringent measures to survey work establishments for study of conditions ; to use this to prevent possible hazards to which workers are exposed.

e. To develop continuous adult education process to keep workers motivated ; to make them aware of their rights and responsibilities.

At the National Level

Children

a. Explore cinema and television as an education media.

b. Work upon strategies for controlling infections affecting children.

c. Medical curriculum must caution against unnecessary prescription of drugs.

Women

a. To give publicity to laws, which protect women from occupational, social, economic and sexual exploitation.

b. To co-ordinate information on cases of injustice and seek redress from authorities at different levels.

People who need medicines

a Press for the use of generic names of drugs, wherever possible and include them with the brand names.

b. To use the media for expression of public opinion for a shift in the licensing and pricing of drugs from the Petroleum to the Health Ministry.

Workers

a. To give publicity to the laws, which protect workers from occupational hazards and economic exploitation.

b. To co-ordinate information on cases of injustice and present them to the respective authorities at different levels.

— Courtesy V.H.A.I., New Delhi

CAUSES OF DIARRHOEA

I *Related to Food and Diet* – the chief being : INADEQUATE FOOD

1) Malnutrition (which increases susceptibility to infection)
2) Bottle-feeding and artificial feeding (associated with the hazards of contamination over dilution).
3) Weanling diarrhoea.
4) Dietary indiscretion – too much food at one time, heavy food.
5) Milk intolerance. Di saccharidase deficiency, especially lactose is often a temporary problem associated with infection or malnutrition.

II *Related to Infection and Poor Hygiene- UNCLEAN DRINKING WATER - POOR SANITATION*

Alimentary

Viruses - Rota viruses commonest – others (other human diarrhoea virus, virus orbi duocrreovenus, measles virus entero virus)

Cause of 10 - 20% of all diarrhoeas in the community. 50% of all diarrhoeas in children between 6 months - 24 months.

Bactreia

Enterotoxigenic E Coli (ETEC) - 25% of all diarrhoeas. One of the common causes of Travellers' Diarrhoea (More common than entero-viral infection - Cecil 1979).

Salmonella In developing countries up to 10% cases among kids.

Shigella Shigella flexneri is common in developing countries. It accounts for 5% causes of acute diarrhoea in under fives.

Vibrio Cholera Accounts for 5 - 10% hospitalized patients in all age groups in non-epidemic cases. Found in children between 2-10 years of age in endemic areas. In epidemics-can affect all.

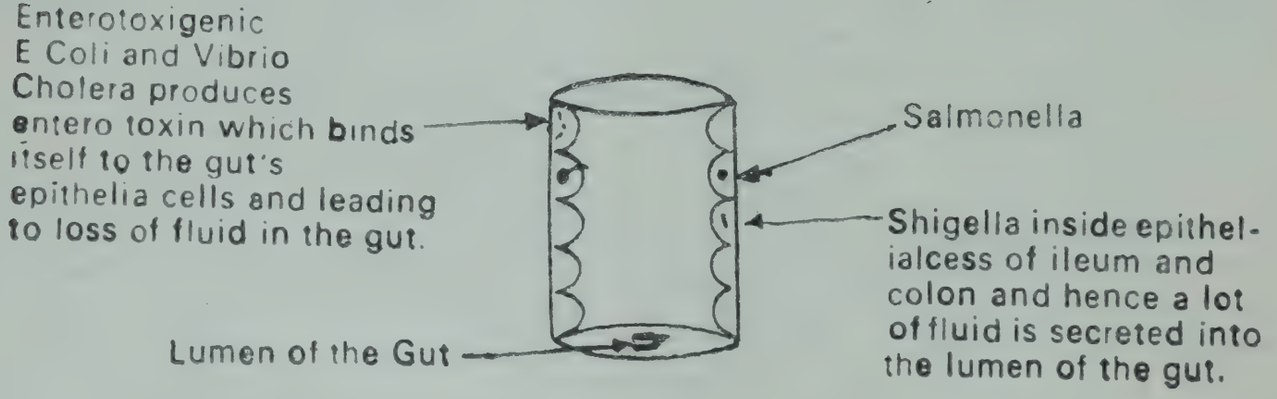
(Others : Vibrio para hemolylocus, enteropathogenic, E. Coli and entero invasive E Coli significance are not known)

Parasites Giardiasis by giardia lamblia Amoebiasis - Entemoebia histolytica.

Systemic infections Upper respiratory infection atitis media, meningitis, malaria, etc.

7-9 litres of fluid are poured as secretions into the *alimentary canal* every day. Most of it is *re-absorbed* ; only 100 - 200 ml. is secreted.

Diarrhoea results if there is *increased secretion or decreased* absorption.

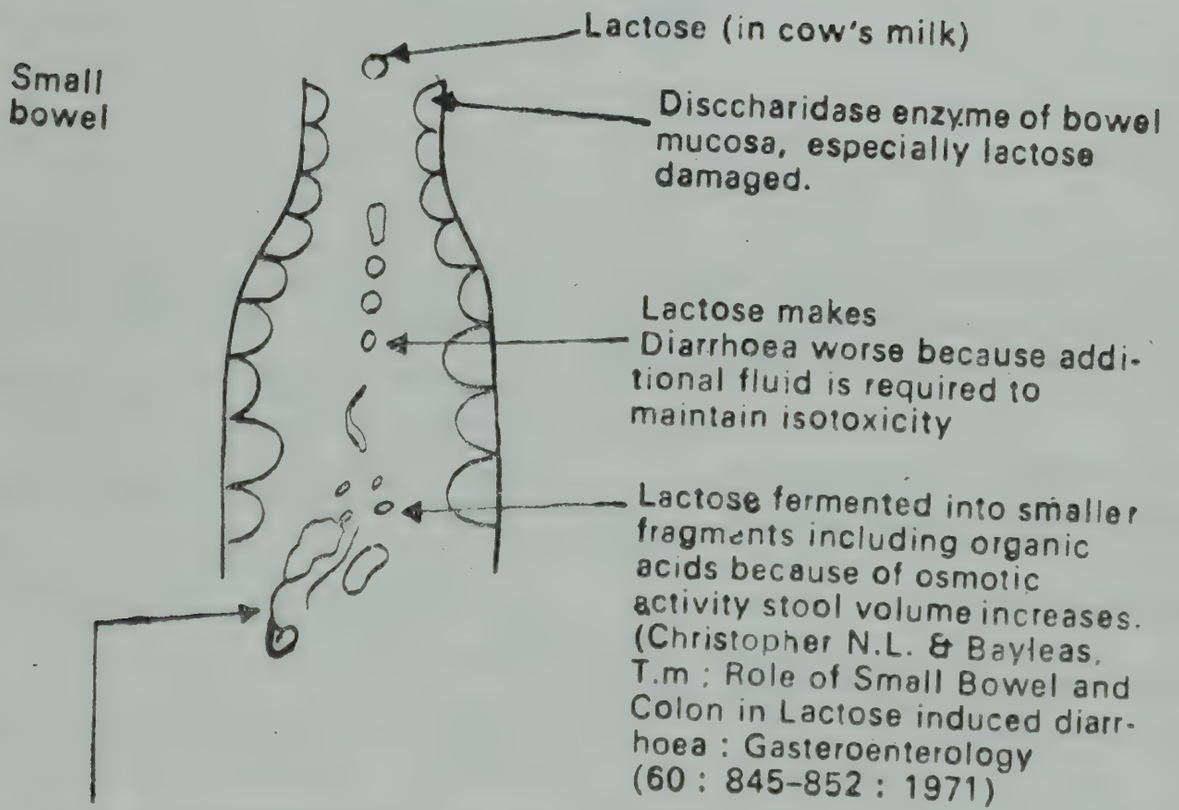


Casuses of death

due to dehydration – loss of water and electrolytes

– sodium
– potassium
– chloride
– bicarbonates
– tolerance

If this is beyond body's capacity.



More Potassium and bicarbonate concentration here than plasma. With the exception of Rota virus the more the stool volume the higher is the sodium concentration in the stool and the greater the sodium deficit. The sodium concentration is the same as plasma, if the rate of loss exceeds 50ml/kg of body weight in 24 hrs.

MAIN CASUES OF DIARRHOEA (page 153 : WHERE THREE IS NO DOCTOR)

Poor nutrition (page 154). This weakens the child and makes diarrhoea from other causes more frequent and worse :

A malnourished child is more likely to get diarrhoea. Is less likely to recover completely and has greater chances of dying.

– virus infection or intestinal flu
– infection of the gut by bacteria (page 131)
– amoeba (page 144) and Giardia (page 145)
– worm infections (pages 140 to 149)

Infections outside the gut –
– ear infections - page 309
– Tonsillitis - page 309
– Measles - page 311
– Urinary infections - page 234

Malaria falciparum occasionally also. Food poisoning, spoilt food (page 135)

Inability to digest milk (mainly in severely malnourished children and certain adults). The difficulty babies have in digesting foods that are new to them.

Allergies due to certain foods-page 166 - occasionally babies are allergic to cow's milk or other milk.

– side effects of certain medicines, e.g. ampicillin, tetracyclin.

Laxatives, purges, irritating or poisonous plants, poisons, eating too much unripe fruits, heavy greasy foods.

Courtesy - V.H.A.I., New Delhi

MANAGEMENT OF ACUTE DIARRHOEA

The major objectives are :

1. Very early replacement of water and electrolyte losses to prevent or to treat rehydration.
2. Maintenance of adequate nutrition to prevent malnutrition.

Early replacement of water and electrolyte losses should commence promptly after the diarrhoea starts. This has three important advantages.

1. It avoids the risk of death from severe hydration.
2. It minimizes the symptoms associated with increasing water and electrolyte deficit, e. g. vomiting, lethargy, anorexia or coma, which interfere with continued feeding.
3. The treatment needed is simple because it is given while two important hemostatics mechanisms (thirst and renal function) are still intact.

Thirst is an important guide to the amount required - any excess salt or water is excreted as long as renal functions are intact.

Maintaining Nutrition - during acute diarrhoea is essential. Except for lactose the gut is capable of absorbing a variety of nutrients. Except for lactose no dietary restriction is needed.

THERE IS NO PHYSIOLOGICAL BASIS TO THE COMMON BELIEF THAT THE 'BOWEL' SHOULD BE RESTED RURING ACUTE DIARRHOEA

IMMEDIATE TERMINATION OF DIARRHOEA by fasting, or giving anti diarrhoeals, etc. is not the primary goal of diarrhoea treatment.

The MAIN consideration of diarrhoeal treatment is that –

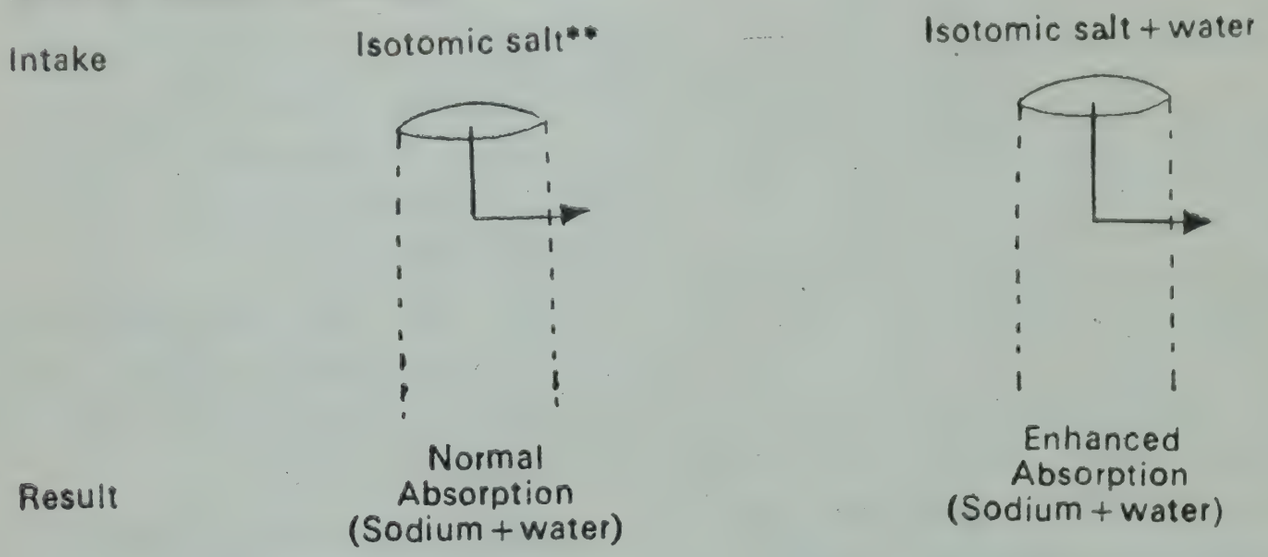
It should be *effective, safe, low cost, encourage self-reliance* and independence in people and be acceptable.

Given the simple, home based method requires adequate communication, education and surveillance. Home preparations involve the mother in the process of her child's health care and this method helps to develop self-reliance and can be given very early.

The problem arises with efficasy of care and safety.

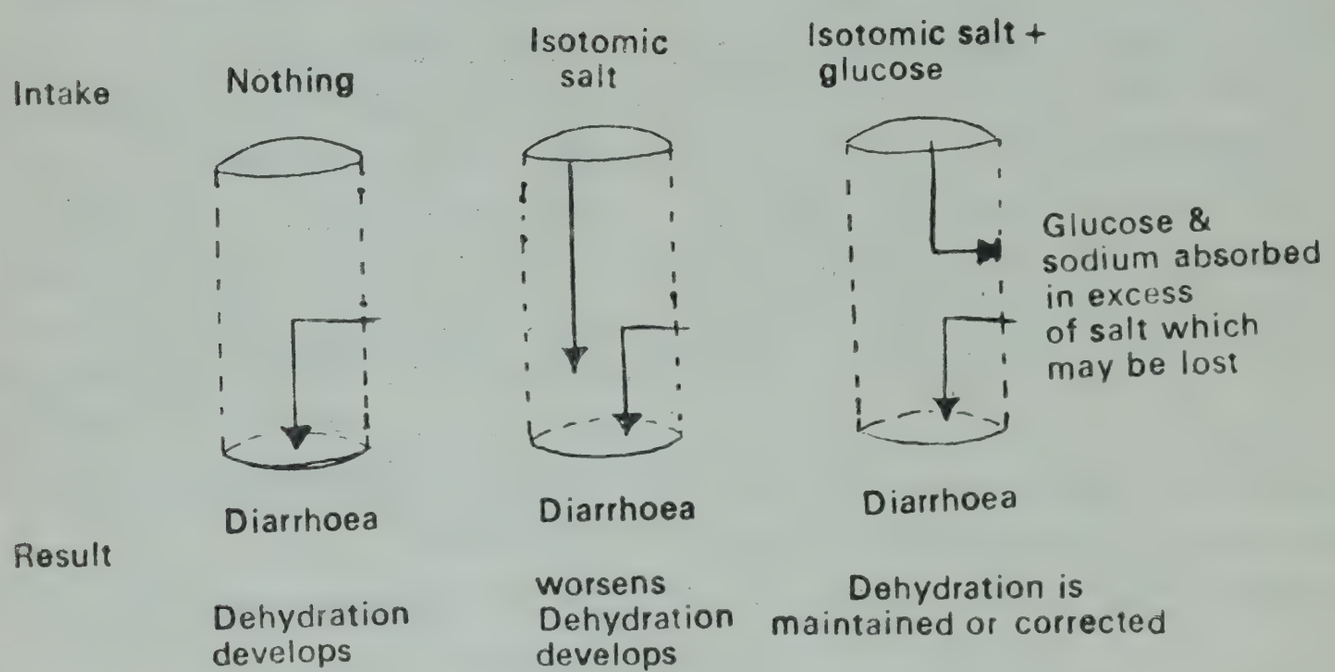
Oral Rehydration Therapy

A. Normal Small Intestine



**Concentration same as in blood.

B. Acute Watery Diarrhoea



Source : Oral Fluid – A simple weapon against dehydration in Diarrhoea. How it works and How to Use it.

N. T. Pierce & N. Hirschhorn
WHO Chronicle 31 - 87 - 93 (1977)

Rehydration Rates By Weight

<5 Kg	50 ml	fast	then 25 ml each hour
5-9 Kg	150 ml	fast	then 50 ml each hour
9-14 Kg	250 ml	fast	then 75 ml each hour
>14 Kg	300 ml	fast	then 100 ml each hour

Fast = 10 - 20 mins.
Adjust for concurrent losses.

Volume of Fluid For Children

For correction of dehydration	20 - 40 ml kg/hr.
For maintenance, i.e., after correction of maintenance	5 ml/kg/hr. + volume of stool in last hour.
Volume of fluid for adults when dehydrated	750 - 100 ml/hour

ORAL REHYDRATION SALTS

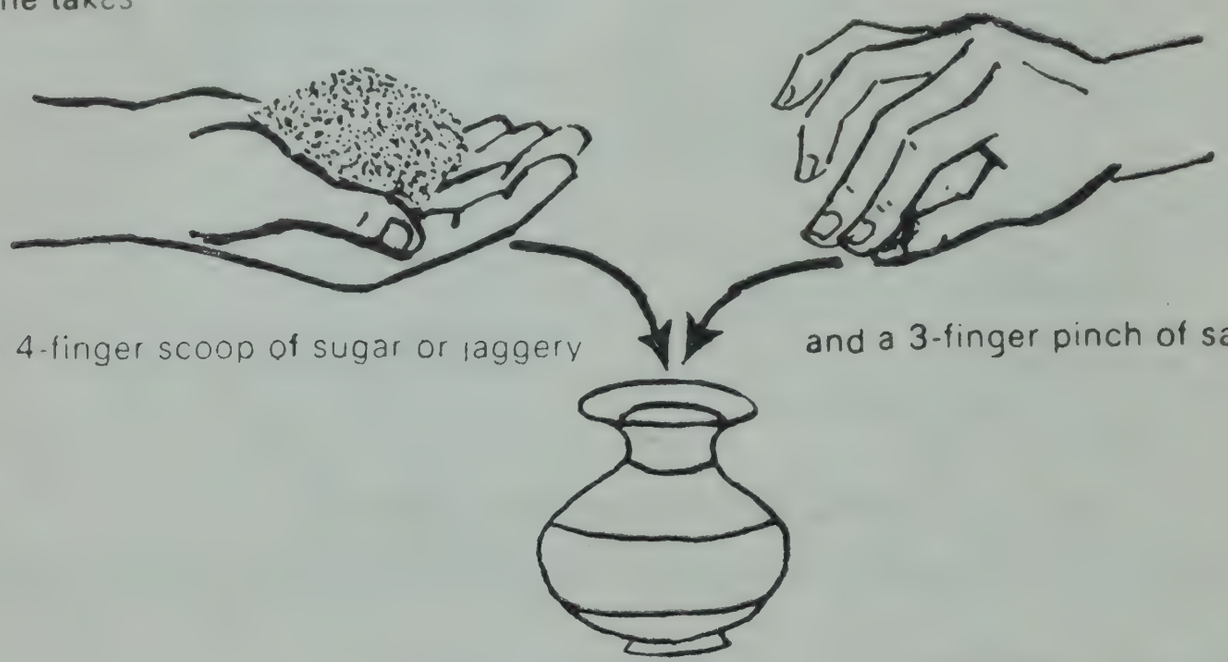
This is an effective and physiologically sound mixture to ensure optimum salt and water absorption.

Preparing the solution

Component	Weight	Approximate domestic weight	Multi mol. per litre
Nacl. Sodium chloride	3.5 gm	1 level teaspoon	Na + 90
$NaHCO_3$ Sodium bicarbonate	2.5 gm	3/4 teaspoon	HCO_3 P30
Kcl. Potassium chloride	1.5 gm	1/2 teaspoon	K^+ 20 cl 80
Glucose	20 gms	8 level teaspoons	Glucose 110
Water	1 litre		

In one litre of water

A mother can also make the Rehydration Drink like this:
She takes



a 4-finger scoop of sugar or jaggery

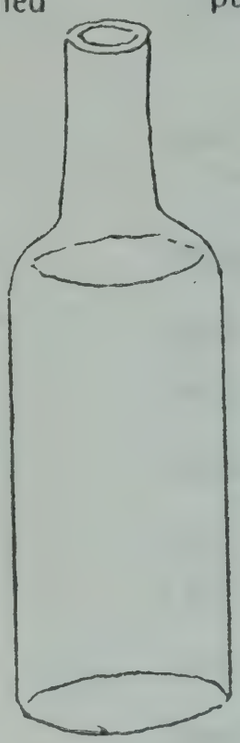
and a 3-finger pinch of salt

and add it to 1 litre of boiled and cooled water.

Rehydration Drink to prevent and treat dehydration

REHYDRATION DRINK—TO PREVENT AND TREAT DEHYDRATION

In 1 liter of boiled water



put

Two tablespoons
– brown sugar
– white sugar
– or honey
– Glucose
(Honey is the best)

and ¼ teaspoon salt

and

½ teaspoon bicarbonate of soda. If no soda is avilable, add another ½ spoon of salt. Lactate citrate or acetate compounds could be substituted for bicarbonate if they prove to have longer shelf life.

If available, add half a cup of orange juice or a little lemon juice to the Drink.

- Do not boil the mixture
- Give sips of the drink every 5 mins. day and night until the person begins to pass urine normally.
- DO NOT GIVE large quantities at one time.
- A small child needs at least 1 litre per day.
- An adult will need three litres or more.
- DO NOT KEEP THE MIXTURE FOR MORE THAN 24 HOURS : specially in the Summer.
- Make fresh mixture daily.

Oral rehydration therapy has been well researched and documented. With cholera and diarrhoea when treated by experienced workers there was *no* mortality and need for I. V. fluids was reduced by 70 - 90% Mortality feel from 25% to only 3.6% during the cholera epidemic amongst Bangladesh refugees in the 1971 war. Treatment was administered by untrained family members, and half of these deaths occurred before the treatment could be started.

(Oral Fluid Therapy of Cholera among Bangladesh Refugees. Johns Hopkins Medical Journal. Pages 132 - 197 - 205, 1973)

SUCROSE : 40 gms sucrose is equivalent to 20 grms. Glucose is preferable to sucrose.

GLYCERINE : An amino acid actively supports glucose and salt absorption. Substituting or adding glycerine might reduse stool volume or frequency of diarrhoea.

GUR : In 20% of patients even after 48 hours of giving salt-gur rehydration therapy, acidosis could not be corrected. Salt-gur rehydration solution for adults with diarrhoea is fine. Probably if acidosis is suspected specially in children it is better to use Glucose or Sucrose.

Which is preferable - Glucose or Sucrose?

Glucose is a simple sugar. It does not require any enzyme to break it down as sucrose does. 40 gms of sucrose (table sugar) is equivalent to 20 gms. glucose. In severe diarrhoeas, glucose is preferable as it is more effective than sucrose.

In mild or moderate diarrhoeas, both sugars are equivalent. Sucrose has to be enzymatically hydralyzed to its component monosaccharide, of which only glucose acts to increase the sodium absorption. Hence, twice the amount of sucrose is required as glucose.

Glucose is more hygroscopic and therefore has to be packed in foil or separate polythene bags. In warm and humid climates (i. e. where there is humidity more than 85%) water absorption by sucrose also is substantial. In the case of sucrose, as enzyme deficiency occurs in some diarrhoeas, sodium absorption will be impeded.

The volume of vomiting or proportion of infants vomiting severely may be greater with sucrose solutions than with glucose.

The choice has to depend upon the relative cost and availability. Glucose is more expensive and less easily available than sucrose table sugar.

REGARDING BICARBONATE
(Baking Soda)

Bicarbonate in the solution (25-30meg/ Litre) as recommended by WHO prevents or reverses acidicis. It improves the appetite and leads to cessation of *vomiting* Bicarbonate is recommended for severe acute diarrhoea.

For routine early rehydration therapy, for mild or early diarrhoeas, the addition of bicarbonate is not considered absolutely necessary (B).

Potassium losses in diarrhoea stools of children tend to be higher than in adults. Replacement of potassium losses is important.

Approximate quantities of selected potassium rich foods required to supplement oral rehydration with a sugar and salt solution.

FOOD	*Amount required per 24 hours*
Banana (raw) mashed : whole (without skin)	1¼ cups — 281 gms.
Large	2 bananas — 256 gms.
Medium	1 2/3 bananas — 261 gms.
Small	3 bananas — 270 gms.
Plantain (raw)	1 plantain — 263 gms.
Coconut water	3 cups — 720 gms.
Lemon juice (raw)	3 cups — 732 gms.
Orange juice (raw)	2 cups — 496 gms.
Papaya mashed	2 cups — 460 gms.
Tomato (raw), ripe	4 2/3 tomatoes — 467 gms.

If the WHO recommended ORS is not available the above foods can be added to the diet.

(NOTE : The above table was devised from data obtained at Hospital Escuela, Legucegalpa, Honduras from Adams)

24 hour requirement based on the amount consumed in complete OR solution during 24 hours by patients with normal potassium levels reported by Clements et al.

REGARDING BOILED WATER

A comparative study conducted in Gambia found that it made no difference to the incidence or duration of diarrhoea whether the water used for ORS was clean or contaminated.

- boiling and cooking is cumbersome specially when there is fuel shortage.
- the people should be told specifically *NOT* to boil the ORS after mixing.
- ORS is a good culture medium for bacteria and hence should be prepared fresh daily. Old, unused preparation should be discarded.

  Feeding with a Cup and spoon is better than bottle feeding.

REGARDING LOW SODIUM CONCENTRATION SOLUTIONS

The arguments against the WHO recommended high sodium formula are :

1. Iatrogenic electrolyte disturbances by way of hypernatremia may be the cost because sodium losses vary,

2. Having a low sodium solution will give a greater margin of safety.

Conclusion of

The Committee on International Nutrition Program Food and Nutrition Board Assembly of Life Sciences National Research Council, WHO. Population Reports. November-December 1980.

Nalin, D. R. Mackenzie, K. Harland and others : Comparison of Low and High Sodium & Potassium Content in Oral Rehydration Solutions - Journal of Pediatrics : In Press; 1980.

- *greater risk of persistent hypernatremia* with lowering of sodium to 60 meq. (instead of WHO recommended 90 meq/Litre)
- Transient elevations of serum sodium occurring with WHO recommended solution is rapidly corrected when feeding commences if no clinical signs of hypernatremia are seen (Jamaican and Indian Study)

It is necessary to over come the danger of hypernatremia (elevation of serum sodium), which is a major problem to be considered in hot climates and in febrile hyperventilation or malnourished subjects.

(Bart, K. J : Finberg, L. Single Solution for Oral Therapy of Diarrhoea : Lancet 2 : 633, 1976).

This is done by

1. Giving additional sodium free water independently (i. e. not mixed with ORS). 1 cup of water with 2 cups of ORS proved safe even in neonates -as shown in a hospital study (B)
2) Breast milk which has low sodium content (only 2-3 meq./lt) can be given alternatively to unweaned infants.

Alternating ORS and breast milk is important nutrition-wise too. Dangers of hypernatremia, convulsions, cerebral haemorrhage and often death.

When to give parenteral I. V. fluids ?

O.R.S. is excellent under most circumstances - under certain specificcon ditions I. V. fluids should be given.

1. A patient with severe dehydratlon. A more than 10% weight loss and showing signs of shock.
2. In patients unable to drink because of stupor, fatigue or coma, nasogastric feeding should be given in sizes.
3. Those with prolonged oligemia or anuria (more than the amount that can be explained by dehydration).
4. Those with severe and sustained vomiting.
5. Those with very severe diarrhoea who lose more fluids than they can absorb, i. e., adults losing more than 800 ml. of stools per hour.
6. In premature infants and babies less than one month old.
7. Those with serious glucose malabsorption (about 3% of all patients)

(Oral fluid - A Simple Weapon against Dehydration in Diarrhoea WHO Chronicle 31. 87-93 : 1977)

Comparison of intravenehous fluid and oral rehydrations therapy Source : ORT. p. 36 and Populations Reports : Nov-Dec. 1990.

Intravenous Therapy	Oral Rehydration Therapy (ORT)
Applicable in all cases requiring rehydration.	Applicable in all cases except where shock or severe vomiting interfere 0-5%
Preventive use not feasible	Easily administered in every case of diarrhoea. If begun early may prevent dehydration.
Requires fixed medical care facility.	Can be prepared and administered in village and home.
Supplies are cumbersome to deliver to the rural areas.	Packets of OR salts are easily distributed. Sugar and salt are available in mosthomes.
Administration requires well trained personnel.	Can be prepared and distributed by minimally trained village workers (preparad by family members)
A narrow range of body tolerance for variations in fluid composition.	A broader tolerance range, but care is still needed for mixing the ingredients.
Monitoring is required to prevent over-hydration.	Early in diarrhoea cases, the satisfaction of thirst usually prevents over-hydration.
Requires sterile preparation and equipment.	Household utensils can be used to mix the ingredients.
Expensive.	Inexpensive.
Trauma and chance of infection from intravenous needles.	There is possible risk in using contaminat water.
Largely, the mother is excluded from caring for the child.	Mother is involved in the care of the child.

Courtesy V.H.A.I. New Delhi

Antimobility drugs

Like opiates,
diphenoxylate
atropine alkaloids
loperomide

The tone and segmental activity of the small intestine. This increases transit time in the bowel,

Harmful organisms which are yielded from the gut by peristalsis continue to harbour. A study showed that diphenoxylate atropine in experimental shigellosis, not only prolonged the diarrhoea and systemic symptoms, but also appeared to contribute to the development of antibiotic induced diarrhoea and pseudomembranous colitis.

Ref: Dupont HI, Hormick RE — A Clinical Approach to Infections Diarrhoea Medicine: 32, 265, 1973.

Stasis resulting from the use of antimobility drugs have several harmful effects:

1. sequestration or secretion of fluid and in the gut lumen may manifest as hypovolemia, even in the absence of overt diarrhoea. A situation which makes the clinical assessment very difficult.

Ref: Fingil E, Freston JW; Antidiarrhoeals and laxatives — A Changing Concept: Clin Castro enterology — 8 : 16, 1979)

2. statistics of fluid in the gut results in abnormal multiplication of bacterial flora with greater chances of invasion of bloodstream.
3. the distension of abdomen resulting from paralytic items may interfere with diaphragm and cause respiratory difficulty.

Walion et al. have seen cases of severe paralytic coma and apnea, etc, due to overdosage of diphenoxylate—side effects resemble morphine poisoning (with which the molecule of diphenoxylate resembles).

These agents are very dangerous for infants who have invasive diarrhoea or paralytic illness.

In acute infective diarrhoea the problem is in the transport pathways of water and electrolytes in the gut wall and not in the mobility hence antiperistaltic agents have no role in such diarrhoeas.

Ref: Gall, D.C.: Hamilton, J. R. — Infections Diarrhoea in infants and children. Chin Gastero enterology 6 : 431, 1977.

Drugs such as opiates, diphenoxylate and loperamide which reduce bowel motility, although widely used, should **never** be given to children. By slowing peristalsis they make the situation worse—this has been seen in a number of children and in volunteers with shigellosis." These drugs also depress respiration and are an important cause of accidental poisoning

— Prof. H. P. Lambert in Diarrhoea Dialogue: February 1982
Drugs and treatment of Diarrhoeal Diseases – Cautious prescription.

Anti-diarrhoeal medicines like Kaolin pectato, Lomotil, Bismuth salts, codeine, etc., act like plugs. They keep in the infected material.

1) The amount of fluid being lost inside the gut lumen cannot be assessed.
2) The infection is prolonged — there is fear of damaging effect on gut lining (bowel mucosa) absorption of toxins.
3) They are specially harmful in infectious diarrhoeas specially those with fever.
4) These drugs are costly and their routine use is not warranted.

Stool thickening agents

Kaolin, pectin, activated charcoal, aluminium hydroxide and bismuth salts.

These drugs do not stop leakage of water and electrolytes from intestinal wall into the lumen The artificially thickened stools may produce a false sense of complacency and hence rehydration is delayed. A study done by Dupont to see the effect of bismuth sub salicylate and placebo in 169 students in Mexico show-

ed no difference in total weight of stools or stool water content.

(Spending Rs. 1–2 per day on pectin -kaolin preparations to improve the cosmetic appearance of stools does not appear worthwhile).

Dupont, HL: Sullivan, P.P. — Pickering, L.K., et al. Symptomatic treatment of Diarrhoea with Bismuth subsalicyclate among students attending a Mexican University Gastro Enterology 73 : 715, 1977.

Antibiotics

In a study by Chandrashekran, et. al they found 35% of their cases had received one or more antibiotic prior to hospitalization.

Ref: Chandrashekharan, R. – Kumar, V. - Murthy, B. – Walia, B.N.S. Carbohydrate Intolerance with Acute Diarrhoea and its complications Acta Pediatr. 16: 449, 1977.

Antibiotics may cause diarrhoea :

1. by local irritation
2. by super infection with bacteria like staphylococci or fungi e.g. Candida.
3. by causing pseudo membranous colitis (amplcillin, gencomycin, calestin or by causing malabsorption — neomycin).

Antibiotics have no role in the majority diarrhoeas as 50–70% of the diarrhoeas are viral.

Antibiotics should only be used :

1) when there is clear clinical suggestion of invasive diarrhoeas (bloody stools and high fever) or cholera (in a cholera endemic area), OR –
2) when laboratory results become available and indicate the need for antibitoic treatment.

Examining Stool

Place small fleck of stool (mucus) on glass slide. Add a few drops of loefflers' methyleis blue stain. Put cover stop. Let it stand for 3 mins. Then examine under microscope.

Foecal Leucocytes +
Shigellosis
Salmonellosis
E Coli
naked eye–blood and mucus

Foecal Leucocytes —
viral diarrhoea
enterotoxigenic diarrhoea caused by V cholera, E Coli watery, profuse, no mucus

R_X Shigelosis

Mild diarrohea (Sonnei or Flexneri dysenteriae) no antibiotic required.

Antibiotic choice should depend upon local experience and sensitivity pattern (eg. Walia et al. report 76% of these bacteria were resistant to tetracyclin, ampicillin, streptomycin and chloramphenicol or combination).

Furoxone and nemoycin EXERT EFFECT ONLY IN GUT LUMEN therefore they cannot be recommended.

Recommended :

Ampicillin 100mg/kg/24hr in 4 divided doses.

Trimethoprim 10 mg sulphamethenazole combination – 50 mg/kg/24 hr in 2 divided doses.

Adults - Tetracyclin 2.5 gms can be given.

Duration of therapy not more than 5 days.

Selmonellosis

Antibiotics should not be routinely used.

Ampicillin and doxacillin therapy prolonged the duration of diarrhoea and time outlines and was associated with increased incidence of bacteriological and clinical relapses.

Ref: Eichenwald, H.E., Mac Cractin, H. Antimicrbiaol Therapy in Infants and children : J. Pediatr. 93 : 35 : 1978)

The use of antibiotics in Salmonella should be restricted to :

1. infants less than 6 months
2. immune compromised infants
3. clinical suspicion of bacteremia

R_x — Ampicillin or chloramphenicol 75–100mg/kg/24 hrs in four divided doses per day for 7–10 days.

Antibiotics in the majority of non-salmonella strains do not change the cause of illness and may actually prolong the period during which stool cultures remain active

— (Prof. Harold Lambert: Diarrhoea Dialogue)

E. Coli

Enterotoxic strains or entero invasive strains. If stools have plenty of leucocytes and E Coli culture groups/entero invasive E Coli inferred and R_x with ampicillin or cotrimoxazole.

If septicemia suspected, parentral gentamycin or kanamycin should be given.

Cholera

Tetracyclin – 50 mg/kg/day in four divided doses for 3 days.

Tetracyclin is found to shorten the duration. Drug resistance is now being seen. An alternative drugs — Furazolidine and Chloramphenicol.

Campylobacter infection

Compylobacter jejuni can cause abdominal pain and mild dysenteric stools by infiltrating the gut wall.

R_x for severe cases —

— Erythramycin — 40 mg/kg/day in three divided doses.

Efficacy unproved.

Giardia

Metronidazole 10 mg/kg/24 hrs X 5 days
Furazalidine 5 mg kg/24 hrs — Is cheaper and equally effective.

Amoebiasis

This can be with or without blood or mucus.

R_x Metramidazole : 40-50mg/kg/24 hrs divided into 3 doses for 10 days.

Neomycin has no role in the treatment of diarrhoea. It cannot only cause renal damage but it can also make diarrhoea dehydration and nutritional losses worse and could interfere with ORT. It has been well established that neomycin reduces intestinal absorption of sucrose, sodium, potassium, nitrogen, fat, iron, lactose, Vit. B 12 and xylose.

In a recent study, Mary Ian Clements showed that neomycin can cause diarrhoea in healthy individuals and prolong it in individuals with E Coli diarrhoea-(Metronidazole if not available, Diodohydroxyguin 40mg/kg/day may be used for 20 days). Recheck stools.

O. R. T.

Total consensus in role of glucose assisting absorption of sodium and water and bicarbonate.

Anti-inflammatory agents

Aspirin and indomethacin prevent secretary effects of cholera toxin. Aspirin 25mg/kg/day decreased foecal losses of water in malnourished children with acute diarrhoea and dehydratino.

Burke, V. Gracey, M. — Reduction by Aspirin of Intestinal Fluid Loss in Acute Childhood. Gastro enteritis: Lancet: 1329, 1980.

Enterotoxigenic E Coli generally cause acute episodes of abdominal pain of relatively brief duration, making antibiotics unnecessary. "Because of the difficulty in identifying these organisims, there seems to be little justification at the moment for treating them with antibiotics. Similarly, for enteropathogenic E Coli. There is no clear evidence that antibiotics are beneficial" — (Prof. H. Lambert in Drugs and Treatment of Diarrhoeal Diseases — Cautious Preparation).

Special Treatment

Take a good history, look for signs, examine stools, then use the following guidelines: As given in *Where There Is No Doctor* by David Werner.

1. Sudden mild diarrhoea — no fever, upset stomach? intestinal flu?

   R_x — lots of fluids

   — no special treatment

   — kaolin pectate can be used for

a plug for adults — never for kids or those very ill.

— if there is colic pain — belladonna.

2. Diarrhoea with vomiting (there are many causes) –

— cholera

— acute gastroenteritis

— food poisoning

(i) fluid replacement give every 5-10 mins.

(ii) for excessive vomiting – promethazine phenobarb AVOID FOR KIDS.

(iii) Refer – if vomiting uncontrollable and dehydration gets worse.

3. Diarrhoea with mucus or blood often chronic, no fever, amoebic dysentery, ulcerative colitis rare.

Rx Metronidazole
Tetracyclin, if no relief – refer.

4. Acute diarrhoea with fever, with or without blood. Bacillary dysentery, typhoid, malaria.

Rx Start treatment with ORS. If fever persists even after 6 hours and seems very ill, give ampicillin If not, give tetracyclin.

If no improvement — refer. If sings of typhoid — start chloramphenicol.

If in a falciparum zone and spleen, start chloroquin.

5. Yellow, bad smelly diarrhoea with bubbles or froth without blood or mucus. Giardia?

Rx — Fluids

— Metronidzzole

(Mepacrine is cheaper but less effective)

6. Chronic diarrhoea — which keeps recurring due to malnutrition, amoebiasis.

Rx — Nutritious food specially rich in proteins.

7. Diarrhoea like rice water — Cholera.

Cholera — Comes in epidemics

— worse in older children and adults

— dehydration is extreme

— vomiting usually precedes diarrhoea.

Rx — ORT

— give double dose of tetracyclin, chloramphenicol.

References

1. Drugs in the Treatment of Diarrhoeas. Dr. B. N. S. Walia, Prof. of Paediatrics, PGI, Chandigarh, Indian Journal of Paediatrics 47: 323-327: 1980.

2. Drugs and the Treatment of Diarrhoeal Diseases: Cautious Prescription. Prof. Harold Lambert: Diarrhoea Dialogue — Issue No. 8: Feb. 1982.

3. Rational Managment in Acute Diarrhoea. Dr. D. D. Joshi of M. F. C.

Cost effectiveness of the different options available and situations in which they may be appropriate

PLAN	ADVANTAGES	DISADVANTAGES	SITUATION
Prepackaged WHO formula	– effective even for severe cholera. – standardized. – highly visible and identifiable – effective for cholera and mild diarrhoea (credibility because it is WHO recommended)	– more expensive – ingredients may not be locally available – can lead to hypernatemia if used incorrectly.	effective for a health system reaching the bulk of the population.
Prepackaged WHO formula with sucrose	may cost less succrose may be more readily available	– less effective for severe diarrhoea – may increase vomiting – ineffective if sucrose deficiency developed.	effective for a health system reaching the bulk of the population.
Local mixing using WHO formula (spoon set)	no dependence on central facilities no packaging costs.	- increased risk of error - storage of ingredients may be a problem	effective for a system of urban and rural clinics with outreach to patients.
Home mixing using salt/ sugar formula (double spoon)	- reduced costs - direct participation of community and family - no dependence on health system. - permits early institution of treatment at home.	- not as effective as WHO formula. - required individual instruction of user. - requires a proper sized container in the home.	effective where majority has no access to a centralized health service but where there is strong community involvement in health.

PLAN	ADVANTAGES	DISADVANTAGES	SITUATIONS
Local mixing using salt/ sugar (no spoons)	- requires no packets, spoons or devices. - minimum investment - encourages self reliance	- measurement of ingredients is more variable. - efficacy of solution cannot be assumed. - requires instructions, standardization and frequent follow-up.	effective where provision of measuring spoons is not practical.
Any distribution scheme using formula with lower sodium content (e.g. 60 meq/L.,)	- decreased risk of hypernatremia.	- Risk of hyponatremia. - Less effective in severe diarrhoea caused by V. cholera or E. Coli	effective where supervision and surveillance is impossible.

Ref : Committee on International Nutrition Programs, Food and Nutrition Board, Assembly of Life Sciences, National Research Council, National Academy Press, Washington DC, 1981. pp. 12–13

BRANDS CONTAINING DIPHENOXYLATE (LOMOTIL)

Antidiarrhoeals

*± Lomotil (Searle)	Diphenoxylate hcl 2.5 mg, atropine sulph. 0.025mg	10-1. 84	Symptomatic relief of diarrhoea	Children above 2 yrs 0.25mg of diphenoxylate hcl/kg body-wt daily in divided doses	Atropine intolerance and jaundice, hypersensitivity to diphenoxylate hcl, diarrhoea associated with pseudo membraneous enterocolitis
*± Lomotil Liquid (Searle)	Diphenoxylate hcl, 2.5 mg, atropine sulph. 0.025mg, alcohol 0.79 ml/50ml	20ml-2.22 60ml-6.59		(Same as above)	
*± Lomofen (Searle)	Diphenoxylate hcl 2.5 mg. atropine sulph. 0.25mg, furazolidone 50mg	10-1. 97	Bacterial diarrhoea with gastro-enteritis or food poisoning	(Same as above)	Hypersensitivity to active ingredients entero-colitis. Hepatic disease, ulcerative colitis and patients on narcotics, addicting drugs or MAOIs alcoholic beverages, G-6PD def.

± Lomofen Susp. (Searle)	Diphenoxylate hcl 2.5 mg, atropine sulph. 0.025mg, furazolidone 50 mg	60 ml-6.75			Hypersensitivity to active ingredients entro - colitis. Hepatic disease, ulcerative colitis and patients on narcotics, addicting drugs or MAOIs alcoholic beverages, G-6PD def.
± Lomomycin (Searle)	Diphenoxylate hcl 2.5 mg, atropine sulph. 0.25mg, neomycin sulph. 250mg	10–5.50	Diarrhoea of bacterial origin associated with gastro-enteritis.	Children above 2yrs Corresponds to 0.25 mg, diphenoxylate hcl/kg body wt. in divided doses	(Same as above)
± Lomomycin Liquid (Searle)	Diphenoxylate hcl 2.5 mg, atropine sulph. 0.025mg, neomycin sulph. 250mg	60ml-10	(Same as above)	(Same as above)	(Same as above)

* MIMS
± CIMS

CONTROVERSIES IN CONTRACEPTION

Edited by S. Moghissi, MD.

STEROIDAL CONTRACEPTIVES AND CONGENITAL ANOMALIES

Excerpts from "Controversies in Contraception" Chapter 4, pages 49 to 59

By Gloria E. Sarto, M.D., Ph.D.

Pregnant women are exposed to exogenous sex hormones (i. e. Androgens, Oestrogens and Progestogens) as a result of one of the following :

1. Hormones usually progestogens, prescribed with intent of preventing a spontaneous abortion
2. Oestrogen and progestogen combination prescribed as a test for pregnancy.
3. The continued use of oral contraceptives through the early stages of an undiagnosed pregnancy.

Teratogenesis depends upon several factors :

1. Specificity of the drug or infectious agent
2. Dosage
3. Time of exposure of the developing embryo
4. Genotype of the mother and embryo
5. Other confounding factors—for example, other drugs and certain disease states.

Some environmental agents acting alone are capable of initiating a process of dysmorphogenesis; however, malformation most commonly is dependent upon a combination of teratogenic agent and the genotype of the individual. Each alone is innocuous but in combination an upset of the dynamics of normal development results in anomalies.

It is evident that our capability to detect a teratogen in man is strongly dependent upon a competent surveillance system. In order to have incidence rates that are reliable, several factors have to be clearly defined. The periods of gestation to be included must be established. Obvious malformations such as anencephaly and cleft lip are easily recognised; internal malformations, however, may go undiagnosed. Transmisson of the information both within the hospital and within the system for collecting the data have potential difficulties.

Recognizing the difficulties in determining teratogenicity in man and the inadequacies of the surveillance system, one can understand why reports in the literature linking a certain drug with an anomaly can vary.

Steroid Hormones and Extragenital Anomalies

Neural Tube Defect :

In 1967, Gal et al reviewed the drug histories of one hundred women who had babies born with meningomyelocele or hydrocephalus and of the same number of control women who had delivered healthy babies. The survey women were on an average some two years older than the controls. As part of the survey the women were asked how the pregnancy was diagnosed. Nineteen women in the survey group and four of the control women reported having received oral tablets, presumably hormones, for the diagnosis of pregnancy. This difference was significant ($P > 0.01$). The tablets most commonly used were Primodos which contain 10 mg of norethisterone acetate and 0.02 mg of ethinylestradiol, and Amenorone Forte which contains 50 mg of ethisterone, 0.05 mg of ethinylestradiol. These authors pointed out the need to examine the role of hormonal preparations as a cause of congenital malformation and as a mechanism to determine pregnancy.

This report was soon followed by another

retrospective study made between 1960 and 1970 (Laurence et al., 1971). In the latter study a related malformation, anencephally, was included. In this series 271 women who had babies with neural tube defects and 323 controls were studied. There was no significant difference in the frequency with which pregnancy tests were used in the survey cases as compared to the controls.

Another report investigating hormonal pregnancy tests and congenital malformations appeared in 1973 (Oaklay et al.). In this study, 433 Atlanta,women who had given birth to malformed offspring were interviewed three months postpartum to acquire family history, socio economic status, etc. There were 123 individuals who had a child with a neural tube defect and of those, ten indicated they had hormonal pregnancy tests. The proportion with positive histories in this group (8.1%) did not differ significantly from the proportion observed in the total group that was studied (10.6%).

Limb defects :

In 1974 Janerich et al., studied 108 cases of genital limb-reduction defects and a corresponding number of controls. The authors defined limb - reduction as the absence of an arm or leg or a part to thereof including absence of fingers and toes. The authors found that 15 out of 108 women with babies who had malformation were exposed to exogenous sex steroids of one type of another as compared to 4 out of 108 controls. The increased frequency among the cause was significant ($P > 0.02$). In 6 of the cases, the women became pregnant while using oral contraceptives, while 6 received hormones as supportive treatment and 3 received sex steroids as a pregnancy test. The same authors, using birth records, looked at secular trends for limb reduction defects. They used two periods of time, from 1968 to 1973 and from 1963 to 1967, during which time oral contraceptive use was lower. When the two time periods were compared they found the total malformation rate of all types had declined about 6% whereas the rate of limb-reduction had increased 33%. In general, it was felt that these data confirmed an association between exogenous sex hormones during gestation and congenital limb-reduction deformities.

Heart defects with or without associated malformation :

1973 study by Levy et al. Prenatal and family histories were obtained from 76 women who had babies with transposition of great vessels (TGV) born from 1942 to 1972. The cases with TGV were matched according to birth dates with control cases who had various Mendelian disorders. Ten of the 76 babies with TGV had been treated with some hormone. Six were treated because of threatened abortion and one was given a hormonal pregnancy test. The other 3 included 2 women who were on insulin and 1 woman who was on thyroid medication. So in 7 of these 76 cases there was no other factor that might cause malformations; this was compared with 76 controls in which there were no malformation. The difference between these two is significant ($P = 0.007$).

In 1975 Nora & Nora initially reported on 19 patients with multiple congenital anomalies from a group of women who had been exposed to estrogen/progestogen compounds or progestogen alone during the vulnerable period of embryogenesis (15 to 16 days of gestation). 4 of the original 19 cases were eliminated. Fifteen patients were eventually considered. The multiple congenital anomalies in this group included those with vertebral, anal, cardiac, tracheoesophageal, renal and limb anomalies described by the anacronym, VACTERL. When they compared the progestogen/estrogen exposure in the VACTERL group during a period of vulnerability with similar exposure any time during pregnancy, the frequency of exposure in the affected group was significantly higher ($P > 0.001$).

From data obtained from the Collaborative Perinatal Project, a prospective cohort

study of 50,282 mother-child pairs, Heinonen et al (1977) reported:

- 19 children with cardiovascular defects born to 1,042 women who received female hormones during early pregnancy (a rate of 18.2/1000 births).
- Among the 49,420 children not exposed in utero to these agents, there were 385 with cardiovascular malformations, a rate of 7.8/1000 births.

This study alleviates some of the biases seen in earlier studies. The drug use was recorded before the birth of the child and the diagnosis of congenital heart disease was made without knowledge of whether or not the individual was exposed. A number of potentially confounding factors such as diabetes mellitus, congenital heart disease in a prior sibling, maternal age more than forty, bacterial infections and many others were controlled. In spite of this, relative risk of congenital heart defect remained appreciably elevated for those who were exposed. Again, the question is whether the hormonal treatment frequently given to women with threatened abortion is the causative agent, or whether the pregnancy had an inherent risk factor that increased the likelihood of anomalies and caused the individuals to threaten to abort. Subtle and unrecognized biases enter at many levels. In spite of this, it would seem prudent to cease pregnancy testing with hormonal agents and discontinue unnecessary use of steroid sex hormones anytime in the pregnancy.

— Courtesy: *V. H. A. I., New Delhi*

REVIEW OF SUPPORTIVE HORMONE THERAPY IN OBSTETRICS

Hormone treatments have been used for the following indications during pregnancy: threatened abortion, recurrent abortion and premature or delayed labour. According to the report of a WHO Scientific Group on "The effect of female sex hormones on foetal development and infant health" (Technical report series 657) :

> "The benefits of progesterone therapies (and of oestrogens) need to be proven before any of these drugs can be recommended for supportive treatment in pregnancy... There is a suspicion that progesterons may be weakly teratogenic or feto toxic."

This report reviews the medical literature on these two points :

A. Efficacy of supportive hormone treatment in threatened and habitual abortion.

B. The teratogenic effects of these hormones on the foetus.

Abortion means the expulsion of a foetus before it reaches viability. The WHO has recommended that a foetus shall be considered viable when the gestation period is more than 20 completed weeks or the foetus weighs 400 gm or more.

About 15% of all pregnancies terminate as a spontaneous abortion. The peak time of spontaneous abortion is between the 6th and 10th week of pregnancy when 65% of abortions occur. This has been connected with a reduced progesterone secretion, as at this time the activity of the corpus luteum is waning and the placental production of the hormone has not reached 'adequate' levels.

The rationale for hormone treatment is based upon observations first made in 1930's that abnormal pregnancies are often accompanied by a relative deficiency of female sex hormones. It was observed that the natural production of oestrogen and progesterone in pathological pregnancy did not increase at the same rate as in normal pregnancy and exogenous female hormones were given in order to supplement the low endogenous hormone secretion. Correspondingly some of the therapeutic regimens involved progressively increasing doses of hormone supplement during pregnancy. In certain cases large doses of oestrogen and/or progesterone were used for short periods in critical situations such as threatened abortions. (A list of common brand names of drugs prescribed for threatened and habitual abortion is attached.)

A. Efficacy of supportive hormone treatment in habitual abortion :

Evaluation of any treatment requires a comparison with the spontaneous cure rate. This fact has always been a major stumbling block in the assessment of regimens used to treat recurrent abortion, since the prognosis of this condition has never been satisfactorily established. The first statistical attempt at evaluation was that of Malpas in 1938. He based his calculations on the assumption that the overall abortion rate consisted of the sum of two independent rates, one due to a non-recurrent (i.e. random) factor, and the other to a recurrent cause. He selected several reasonable combinations of incidence rates for these two factors and calculated the expected abortion rates.

At a later date, Eastman and Hellman used the same formula to calculate the prognosis from incidence rates which they felt were more realistic. These theoretical calculations are summarized in *Table I*. If one assumes, for example, that the recurrent abortifacient factor has an incidence of 8%, and the random frequency of abortions has one of 10%, and if there has been one previous abortion, then the formula predicts a 50:50 chance of there being an abortion in the next pregnancy. Unfortunately, it has often been forgotten that these are

simply theoretical predictions which require substantiation by careful, well-designed experiments. Instead, if some regimen yielded a pregnancy salvage rate better than the predicted one, this has been taken to constitute "evidence" of therapeutic effectiveness. The fallacy of such thinking was emphasized in a review of the problem by Goldzieher and Benigno. From the inadequate and highly variable data which could be collected, it appeared that the incidence of abortion after two previous abortions was 23% (not 12.6% or 13.2% as predicted). After three consecutive abortions it did not rise to 38% as expected, but remained at about 24%; and after four consecutive abortions it did not rise to 73 to 84% as predicted, but remained just under 40%. Finally the observed abortion frequency remained at this figure even in patients although the Malpas formula predicted that the abortion rate should approach 100%. When one considered other cases, in which there had been term pregnancies prior to the series of abortions, the discrepancy between theory and observation was even greater. No tendency whatever for the abortion rate to rise with increasing numbers of previous abortions was observed. Unfortunately, the published data on abortion incidences in untreated patients were so variable that no statistically valid prognosis could be estimated. Goldzieher and Benigno pointed out that the only way to evaluate therapeutic effectiveness would be by double-blind placebo techniques, with the reservation that a high spontaneous salvage rate might make such a comparison impractical because of the large numbers of patients required to enable the investigators to distinguish between spontaneous salvage and therapeutic benefit.

Table I: Predicted abortion incidence after one to four successive abortions as calculated from assumptions.

Assumed abortion incidence, %			
Due to Recurrent cause	Due to Non-recurrent cause	Previous successive abortions. No.	Predicted Abortion Incidence, %
8	10	1	50
		2	91
		3	93
		4	99.7
2	16	1	25
		2	53
		3	85
		4	97
1	17	1	13
		2	38
		3	73
		4	94
0.4	9.6	1	13
		2	37
		3	84
		4	88

Misinterpretations of the Malpas calculation continue to appear, as in the studies of Goldfarb and Gongsaki with norethynodrel. Some investigators have lumped threatened and habitual abortion together in their evaluations – a procedure of doubtful merit – or have reported the superiority of the progestin over another from data not even subjected to a simple statistical test such as chisquare analysis, which, in fact, shows that the differences observed can be explained equally well by pure coincidence. Seidl et al, instead of using a placebo, compared oral progesterone with 19-norsteroid administration. The former group showed a 21% abortion rate and the latter a 71% abortion rate – a significant difference. They concluded that progesterone was of therapeutic benefit. Another equally valid conclusion might be drawn from these data, namely, that progesterone treatment has no value at all, and that 19-norsteroids are harmful.

Data presented below indicate that the latter inference is probably the correct one.

I. The first investigation to approach the problem of recurrent abortion in a statistically sound fashion was *the double blind study of Sherman and Garrette.*

The purpose of this study was to present the result of a double blind study of treatment with a progestogen in 50 patients selected for treatment on those individuals showing evidence of a low or declining progesterone production. If progesterone treatment is of material assistance to these individuals then there should be a significant difference in the salvage rate from those receiving an adequate dose of the active preparation compared with those receiving placebo. 50 patients with two or more consecutive previous abortions with a persistent low or declining pregnanediol excretion in the current pregnancy were selected (patients showing uterine reduplication or persistent normal levels of pregnanediol excretion were eliminated from the study).

All 50 patients received injections of either solution A or B, one of which contained *hydroxy progesterone caproate* and the other only the injection medium. Of those receiving solution A, 18.5% aborted. Of those receiving solution B, 21.7% aborted. They concluded that

> "The overall incidence of foetal wastage is 20% whichever of these solutions contain the progestogen. These results do not so far support the claims that progestational therapy is of specific value in the prevention of abortion. Of the six aborters examined, four were grossly abnormal."

II. The second double blind trial was conducted by Joseph W. Goldsieher. 54 habitual aborters (those with 2 or more previous abortions) with low or normal pregnanediol excretion were selected. The drug used in this study was *medroxy progesterone acetate.*

"The habitual aborters with a low pregnanediol excretion have a spontaneous salvage rate of about 80%. This favourable prognosis places the gravity of the problem of habitual abortion in an entirely different light. It may also explain the curious coincidence that a great variety of gynaecological, endoerine, or psychotherapeutic treatments have all achieved the same level of therapeutic benefit – a salvage rate approximating 80%. This high spontaneous salvage rate makes it virtually impossible to prove the therapeutic efficacy of a drug used to treat habitual abortion. The data of our study provide no evidence for a difference in the prognosis of habitual aborters with low pregnanediol excretion as contrasted to those in whom pregnanediol excretion is normal."

The study concluded with a comment that "If one excludes well-defined causes of recurrent abortion such as cervical incompetence, the scarcity of "idiopathic" habitual aborters becomes noteworthy. It may be timely to raise once again the question whether there is any such disorder as habitual abortion at all or whether it is merely the unfortunate result of chance coincidence."

III. The third double blind study was conducted by Arnold Klopper and Malcolm MacNaughton.

Two groups of patients were studied. The first, consisting of 33 individuals were the subject of the therapeutic trial; the second consisting of 41 individuals did not have any hormone therapy but, like the first, had urinary steroid assays done. Both groups were subject to recurrent abortion having had 2 or more abortions and never having carried any pregnancy beyond 28 weeks. A point of cardinal importance was that they should come under surveillance very early in pregnancy. In a previous publication, MacNaughton (1961) had shown that in their hospital population more than half the patients who abort do so before the 12th week. Any group of patients of whom a considerable proportion are more than 10 weeks advanced in pregnancy when they first come under study is a group heavily biased toward spontaneous success. In this series nobody was accepted for trial who was more than 10 weeks pregnant.

The drug chosen for administration was *cyclopentyl enol ether of progesterone* as it is the only artificial gestagen which is like progesterone metabolizes to pregnanediol in the body.

The study concluded that: "It is unlikely that the wrong compound has been chosen for trial. It is more probable that the element in abortion which can be corrected by exogenous progesterone is a very small one and that very few pregnancies will be salvaged by this means. Much of the apparent success of progesterone therapy in the past may be due to the fact that proper blind therapeutic trials were not done and that the steroid administration was begun at 10 to 14 weeks of pregnancy; a stage when the danger of abortion is largely past. It is possible that foetal chromosomal abnormality, rather than excessive myometrial contractility due to hormone deficiency, is the most frequent cause of abortion in early pregnancy.

Too much emphasis has been placed on the prognostic value of hormone estimations. It seems more probably that a reduction in hormone production is an effect rather than the cause of abortion and that in the majority of cases, when a lowered pregnanediol occurs the pregnancy is already beyond salvage."

IV. Study by R.R. Macdonald et al. Cervical mucus ferning indicating some degree of hormone deficiency was observed in 40 of 56 patients with recurrent abortion. These 40 patients were treated with oral *dyhydrogesterone* on a double blind basis. 85% of the patients delivered healthy babies, but no direct effect or improved result could be seen when the active drug was used.

They recommend a clinical plan for specific treatment of women with a history of recurrent abortions.

- At the first visit, as early in pregnancy as possible, a mucus sample is taken from the lower endocervical canal and a cytology smear from the lateral vaginal wall (the cervical mucus and vagainal cytology smears are simple to collect,

cost less and give an assessment more quickly. They are of greater clinical value in demonstrating for more deficiency and in assessing progress).

— Urine is collected for a gonadotrophin pregnancy test. The results of the mucus test for ferning and of the pregnancy test are available before the patient leaves the clinic the same day.

— Specific assurance is given that regular attendance at the clinic with correction of any detected abnormalities will give the patient at least an 80% chance of a live child in that pregnancy regardless of her history.

— An oral tablet to be taken twice a day is prescribed and the patient is told that it will help her maintain the pregnancy : regular psychologic reinforcement is, we believe, of specific benefit – at present folic acid tablets are prescribed.

— This is repeated every week to 14 weeks and then every 2 weeks to term.

B. The teratogenic effects of these hormones on the foetus :

(Excerpt from report of a WHO Scientific Group, No. 657)

Risks to offspring : Concern about possible hazards to the fetus exposed to various sex hormones provided as supplements during pregnancy dates back to a report of masculinization of a female fetus as a result of exposure to 17-a-ethinyl-19-nortestosterone. These observations have not been reported from studies designed specifically to identify adverse fetal effects. Other adverse effects of this exposure have been recognized in both female and male offspring following recognition of the occurrence of clear cell adenocarcinoma among young women with a history of in utero exposure to diethylstilbestrol. In female offspring other adverse effects are adenosis of the vagina and cervix, which occurs in a high proportion of the exposed and an increased risk of prematurity in their pregnancies. Also observed have been alterations in the shape of the uterine cavity as documented by hysterosalpingography. Among the male offspring, there have been reports of epididymal cysts and abnormalities of sperm number, morphology, and motility.

Possible risks to the fetus of exposure to steroidal sex hormones are difficult to study and published studies are difficult to evaluate. Some have argued that the question of the safety of progesterone is distinct from that concerning other progestogens since the oocyte and embryo are exposed to physiologically high concentrations of endogenous progesterone during pregnancy. There is an "intuitive belief that progesterone must be safe." However, some researchers have questioned "whether exogenous progesterone has an effect on the body physiologically and biochemically different from the effect of endogenously produced progesterone."

The effects on the health of the fetus of the underlying conditions for which exogenous hormones are given need to be separated from the effects of the hormone itself. Case series without adequate controls have been reported, some showing no increase in malformations and others an increase.

In respect of several studies it is not readily possible to separate sex hormone support therapy from other hormone exposure such as hormonal pregnancy testing or inadvertent use of contraceptive steroids. Moreover, in many of the reports information on exposure is insufficient to allow the reader to distinguish between progestogens, progesterone, estrogens, or combination preparations.

Studies that report mainly on hormonal

support therapy are summarized in Tables 2 and 3. Table 2 lists several case-control studies in which the use of supportive hormones during pregnancy has been compared for mothers of malformed children and those of normal children. In some studies the control mothers had infants with certain abnormalities, such as gastric disorders, which were thought to be unrelated to hormone use. Recall bias is not excluded in several of the studies and in many the selection of controls can be criticized. In some, inadequate attention is paid to confounding in the analysis. None of the research groups attempted to identify the underlying condition that led to the choice of hormonal therapy or its possibly independent effect on the pregnancy outcome.

Three of the 7 studies reported a significant increase in the relative risk of various malformations associated with hormonal support therapy. In 2 of these studies the malformations investigated were congenital heart disease and the other considered limb-reduction deformities.

The results of 5 cohort studies are summarized in Table 3. In these the investigators compared the rates of congentally malformed children among mothers with a history of exposure to supportive sex hormones during pregnancy with rates among unexposed mothers. A small increase in risk of congenital malformations was observed in the exposed group in 3 of the 5 reports.

The findings from these various studies do not rule out the possibility of a small increased risk of congenital malformations, especially of the heart, among children exposed to supportive sex hormone therapy during pregnancy. Since the risks observed in these studies were small it is impossible to determine whether they could be explained by the confounding effects of demographic variables or by the health effects of the underlying condition for which the woman received hormones. Moreover, the effectiveness of sex hormone therapy during pregnancy is still unproven.

Contd . . .

Table 2 : Case-control studies on possible association between supportive sex hormone therapy and congenital abnormalities

Author	Type of abnormality	Abnormal cases (and % exposed to hormone therapy)	Normal controls (and % exposed to hormone therapy)	Odds ratio	Comments
Nelson & Forfar	Various congenital malformations	458 (4.1%)	911 (2.9%)	1.4	Includes corticoids and thyroid
Levy et al.	Transposition of great vessels	76 (13.2%)	76 (0.0%)		Control series of Mendelian disorders matched for date
Janerich et al.	Limb-reduction defects	108 (8.3%)	108 (2.8%)	3.0	Recall bias possible
Yasuda & Miller.	Transposition of great vessels	58 (1.7%)	93 (2.2%)	0.8	Control series of limb-reduction deformities collected at a different time from case series
Hellstrom et al.	Limb-reduction defects	32 (12.5%)	30 (3.3%)	3.8	Control series of spina bifida
Jenerich et al.	Heart defects	104 (5.8%)	104 (1.0%)	5.8	Recall bias possible
Rothman et al.	Heart defects	390 (3.7%)	1254 (2.4%)	1.5	Recall bias possible

Table 3 : Cohort studies on possible association between supportive sex hormone therapy and congenital abnormalities

Author	Type of abnormality	Exposed to hormones (and rate/1000 abnormal)	Not exposed (and rate/1000 abnormal)	Relative risk	Comments
Harlap et al.	Various congenital malformations	432 (108.8%)	11036 (77.6%)	1.4	A few cases with abortifacients included
Kullander & Kallen	Various congenital malformations	112 (125.0%)	4904 (129.7%)	1.0	
Goujard & Rumeau Rougette	Various congenital malformations	830 (18.1%)	10157 (16.3%)	1.1	
Heinonen et al.	Various congenital malformations	866 (86.6%)	49416 (64.2%)	1.3	Exposure to progesterones
		614 (71.7%)	49668 (64.5%)	1.1	Exposure to estrogens. About 20% of exposed were only to oral contraceptives
Heinonen et al.	Heart defects	1042 (18.2%)	49240 (7.8%)	2.3	About 20% of exposed were exposed only to oral contraceptives.

	Brand Name	Manufacturer	Compound	Threatened abortion	Habitual abortion
1.	DUPHASTON	Duphar Interfran	Dyhydrogesterone 5.0 mg tab.	√	√
2.	FARLUTAL	Walter Bushnell	Medroy progesterone acetate 5.0 mg tab.	30-60 mg daily	20-40 mg daily
3.	GESTANIN	Organon	Allylestrenol 5 mg tab.	5 mg t.i.d. for 7 days	5 mg once or b.i.d. as soon as pregnancy is established. Treatment to be continued at least a month after the critical period.
4.	LUT ESTRON FORTE	Mac.	Progesterone 25 mg oestradiol dipropionate 3 mg. per ml; amp.		1 amp. weekly until a few weeks before delivery.
5.	PROLUTON DEPOT	German remedies (Schering)	Hydroxy progesterone caproate 125 mg & 250 mg/ml. & 500 mg in 2 ml amp.	√	√
6.	OSTERONE	Lyka	Progesterone 25 mg oestradiol benzoate 2.5 mg, per ml.	√	√

Source : CIMS, May 1982.

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3. "Hormones in recurrent abortion" Arnol Klopper and Maecolm Mac-Naughton. Journal of Obstetrics & Gynaecology. 72; 1022; 1965.

4. "Double blind study of effect of 17 hydroxy progesterone caproate on abortion rate" Sherman & Garrett. British Medical Journal 2 Feb. 1965, 292-295.

5. "Cervical mucus, vaginal cytology and steroid excretion in recurrent abortion" Macdonald et al. Obstetrics and Gynaecology Vol. 40, No. 3, Sept. 1972. 394-402

Courtesy : *V. H. A. I., New Delhi*

THE CLIOQUINOL CONTROVERSY

Demanding its ban. A Just Demand. Or, Just a Demand ?

We are grateful to our friends in IOCU, Penang, Social Audit, UK, for Some valuable information they sent to us.

Historical Background

Hydroxyquinolines were introduced into the Swiss Pharmacopea in 1900 as a *topical and antiseptic agent.* In the 30's it became a focus of interest when its potential as an intestinal amoebicide was investigated.

It was around 1932 that classical animal studies established the "therapeutic potential of the halogenated hydroxyquinolines as *lumenal amoebicides*"

i) Ref : Leake, C. D. (1932) Chemotherapy of Amoebiasis. Journal of American Medical Association - 98. 195-199.

The initial clinical trial of clioquinol was conducted in the U.S.A. in 1933.

ii) David, N. A., Johnstone, H. G., Reed, A. C., Leake, C. D., 1933. The Treatment of Amoebiasis with todochlorhydroxy-quinoline (vioform N.N.N.). *Journal of American Medical Association. IOU. 1658 - 1661.*

Data cited in this report suggested "the compound might have a useful spectrum of action against other enteropathogenic protozoa and bacteria".

Since then "halogenated oxyquinoline derivatives HOQ" have been popularly used for prophylaxis and treatment of gastroenteritis, amoebiasis, travellers' diarrhoea (HOQ include a todochlorhydroxyquinoline, proxy quinoline, halquinol, diiodohydroxyquinoline, chlorquinaldol chiniofon).

In 1934 the first proprietary preparation was promoted to the public for treatment of amoebic dysentry and simple diarrhoea.

As a result of a chance clinical observation, hydroxyquinolines became established for twenty years for the treatment of *acrodermatitis enteropathica* (a rare skin disorder) until it was shown that it acted by rectifying the underlying selective malabsorption of zinc by forming an absorbable chelate and it was replaced by zinc.

WHEN WERE THE INITIAL OBSERVATIONS ABOUT CLIOQUINOL RELATED PROBLEMS NOTICED?

According to Dr. Ole Hansen, in 1935, the very first year after C I B A (of Switzerland) had started marketing the drug - "a report from doctors in Argentina describing exactly the same side effects as the Japanese cases in the 60's and 70's was received by CIBA".

"From internal documents in 1939, from Switzerland and documents released in the courts in Japan, it was discovered that experiment of the drugs with cats and dogs had proved fatal".

"In the early 60's, a Swiss and a Swedish veterinarian reported to CIBA GEIGY that they had found dogs with diarrhoea treated with Enterovioform had died, in seizures".

According to Dr. Ole Hansen "attempts to hide facts," (e.g. denial that the drug is absorbed) and attempts to convince doctors not to publish their negative experimental findings have been made throughout by CIBA GEIGY, the producers of Mexaform and Enterovioform.

Even before or during epidemics of SMON in Japan, several reports regarding systemic toxicity following partical obsorption with oral administration was recorded.

Cases of optic atrophy were observed in

a small proportion of children receiving the treatment for acrodermatitis enteropathica- this was prolonged in high dosage treatment. Since earlier, children never survived without treatment, optic atrophy as a late manifestation of the disease could not be excluded.

In 1964, reversible and unusual gait changes were noted in 20 out of 4000 institutionalized patients on long term treatment.

(Ref: Gholz, L.M., Arons, W.L. (1964): Prophylaxis and Therapy of Amoebiasis and Shigellosis with Iodochlorhydroxyquin.

American Journal of Tropical Medicine and Hygiene. 13: 396-401).

Convulsions in laboratory mice on high dosages was reported in 1969 and in "domestic dogs and cats treated for diarrhoea in veterinary practice"

A reversible confusional state had been described following acute dosage in man.

Five personal observations of "transient global amnesia after clioquinol" have been reported in the Journal of Neurology, Neurosurgery and Psychiatry 1979: 42, 1084-1090 by M. Mumenthaler, H. E. Kaiser, A. Meyer and T. Hess from the Department of Neurology, University of Berne and Basel, the State Hospital, Lucerne and the Department of Internal Medicine, Berne, Switzerland.

According to WHO's Drug Information: Jan-March 1978, though sporadic cases for about 6-7 years were reported, it was only after three decades of use of "clioquinol in the treatment and prophylaxis of diarrhoea in Japan that SMON was recognized as a distinct clinical entity in 1964 (Tsubaki, T., Toyokura, Y., TSU Kagoshi, H. (1965). Sub-acute Myelo Optic Neuropathy following abdominal symptoms - A clinical and pathological Study, Japan Journal of Medicine: 4, 181 - 184).

HOW USEFUL IS CLIOQUINOL?

There in evidence to suggest that clioquinol is effective in the prophylaxis of travellers' diarrhoea.

British National Formulary, 1981

The claim for the value of clioquional in the prevention and treatment of that nebulous ragbag "travellers' diarrhoea" do not withstand critical examination.

The Lancet (1977)

The Committee (on Safety of Medicines, UK) has reviewed the data relating to the efficacy of clioquinol in the treatment of diarrhoea and considers "that there is inadequate evidence to support the claim".

Pharmaceutical Journal (30-7-77) Page 597.

The drug was excluded from consideration by a WHO expert committee convened in 1977 to prepare a model list of "essential drugs" on the *grounds that the risks of treatment out-weighed the potential benefits.*

(Ref.: WHO 1975: Selection of Essential Drugs. Techn. Ref. Series 615 page 14).

The editorial in the Journal of American Medical Association 10th April 1972, page 273 stated:

". . . . in the 40 years that clioquinol has been available only one study which is not entirely convincing, has shown it to be effective in preventing travellers' diarrhoea whereas one other prospective study has shown it to be no more effective than a placebo. . . ."

"Hydroxyquinolines are active only on organisms presents *within* the intestinal lumen. Used alone, therefore, they are

active only in the absence of significant tissue invasion — a development that cannot be excluded with certainty even in patients with asymptomatic amoebiasis".

PDT/DI/78.1 WHO : Drug Information Jan-March 1978

Anti-diarrhoeal drug blinds and damages brain – M. V. Kamath, Times of India, 20th June 1977.

"The scientific evidence for the value of clioquinol in the treatment or prevention of traveller's diarrhoea is scanty".

According to Dr. P. C. Pandiya of Jaipur, then President of the Pharmacy Council of India. "The Indian brand of Mexaform contains 2 more drugs (besides Iodo chloro hydroxyquinoline the basic drug phanquone and oxyphenonuin - and has come to be used not only for travellers' diarrhoea but diarrhoea of all descriptions including that due to indigestion".

"The dramatic relief is due to oxyphenonuim which reduces the spasm of the intestines and bowel movements and thus markedly reduces abdominal pain and discomfort".

The Hathi Committee had included clioquinol in the analogous list of essential drugs, "Due to its low cost in relationship to alternative treatment and having regard to the paucity of documented evidence of SMON within the country".

But in India Hydroxyquinolines are supposed to be obtained only under prescription (like many other drugs). How much this restricts the vigorous selling of the drugs over the counter is well known to all of us.

What is Smon ?

SMON stands for Subacute Myelo Optic Neuropathy.

"In its classical form the condition was characterized by the prodermal gastro-intestinal symptoms considered to be of neurogenic origin.

- an ascending numbness of both legs associated with severe and persistent dyaesthesiae.

- frank myelopathy revealed by exaggeration of reflexes extensor plantar responses a sensory level in the trunk and sphincter disturbances could also occur and the combination of exaggerated patellar reflexes and absent ankle jerks was considered to be a characteristic finding.

Disturbances in visual acuity developed but they were not usually an early manifestation.

The increase in the number of SMON cases reported annually were substantial. In 1965, 451 cases were reported and in 1969 the number went up to 2340.

(PDT/DI/77.4 page 10) : WHO-Drug Information. 1977

"Females and elderly were particularly vulnerable and formed a high proportion of patients who also suffered from serious chronic diseases".

(Ref. : Sobur, I.,Ando,K., (1969)-Review and Comment on Myelo Neuropathy Accompanied by Abdominal Symptoms, Paisnin Igaku 24, 2390 - 2397.

More reports were received in summer- "A correlation between the use of clioquinol and the occurrence of SMON in a series of 171 patients was first reported in 1971".

(Ref. : Taubaki T. Honma; Hoshi, M.-(1971) : Neurological Syndrome Associated with Clioquinol : Lancet 1, 696 - 697.

This was following the discovery of a green compound-later identified as an iron chelate of clioquinol on the tongue of some patients and in the urine and faeces

of others by Professor Tsubaki of Sigata, Japan.

Regarding the effect of SMON which, according to some clioquinol sympathisers, have allegedly been due to *idiosyncrotic causes* the relationship between SMON and Clioquinol has unequivocally been shown.

According to the WHO report the fact that some 15% of the victims had apparently never taken clioquinol may merely reflect the difficulty in obtaining precise drug histories from patients; alternatively, it may indicate the existence of other factors in the etiology of the disease, or that SMON may not always be readily distinguishable on clinical grounds from other neuropathies.

Pharmaceutical Journal
30.7.77 : page 597

Similarly, the reasons for having detected less number of cases before 1955 could be attributed.

- to a low detection rate
- the absense of an unidentified aetiological co-factor
- relatively low volume of sales
- relatively low dosage and duration of treatment
- or to the existence of poorly absorbed formulations

The effect of particle size and presence of emulsifying agents on the absorption of clioquinol, could have a bearing on the discrepant results of long term toxicity test on animals.

Social Audit's leaflet on Cliquinol :

"Bad information means bad medicine" has this to say about SMON :

"Clioquinol has caused thousands of cases of SMON a condition involving continuous pain, paralysis, blindness and, in extreme cases, death. In Japan, cases of SMON reached epidemic proportions—affecting an estimated 10,000 - 30,000 people before the drug was banned there in 1970".

The casual relationship between clioquinol and SMON has even been accepted by the Japanese courts.

What is the incidence of SMON outside Japan?

According to a Lancet editorial of the 28th May 1977, page 596, "the companies deny that the neurological damage from clioquinol is a serious risk outside Japan and identical abnormalities of the nervous system have been reproduced in animals".

According to the Journal of the American Medical Association : "The absence of epidemics in other countries does not invalidate the conclusion that clioquinol is neurotoxic. Clinicians from England, Australia, Switzerland, Sweden, Denmark, the Netherlands, and the USA, have described patients who developed neurological symptoms while taking these compounds.

The clinical symptoms of these patients were like the one that characterized SMON".

Journal of the American Medical Assn.,
23rd July, 1973 : Page 296

According to an international survey on recent reports concerning intoxications with halogenated oxyquinolines derivatives — "A survey of the literature has proved that 86 cases were reported as SMON or intoxication of halogenated oxyquinoline derivatives (including suspected cases in 47 articles published outside Japan from January 1970 to February 1977).

According to Dr. N. H. Wadia in his article : "Some Observations on SMON" from Bombay in the Journal of Neurology. Neurosurgery and Psychiatry 1977 : 40, 268-275 where he reported 9 cases of SMON by retrospective study of their

hospital records from 1967 - 71 and prospective search from March 1972 till 1977.

"In 1977 it would be imprudent totally to ignore the Japanese experience. If the factors which makes for the reported difference in SMON prevalence is genetic, SMON may never appear in India in epidemic form. But, if the factor is environmental or infective then the change in the Indian environment may result in the appearance of SMON".

(The above study was funded by CIBA GEIGY).

CIBA GEIGY one of the two main manufacturing companies of hydroxyquinolines has collated details of about 200 possible cases – published as well as unpublished.

The total number of cases of SMON reported from outside Japan is less than 100, of these a high proportion are from Australia.

Clioquinol - Restrictions, Bans, Boycotts

Hydroxyquinolines are sold in more than 100 countries. In some, there is a ban on its sale while in others sale is restricted to prescriptions.

Some of the countries which have imposed restrictions are Australia, Denmark, Venezuela and Norway. In the Federal Republic of Germany, Finland, France, "Traveller's Diarrhoea" has been deleted from recommended indications and the compound has been placed on prescription.

More Specifically :

SWEDEN : At first, HOQ was accepted for treatment of acrodermatitis enteropathica. Later, however, Sweden totally withdrew it and replaced it by zinc salts, which is considered safer and more efficacious.

In the summer of 1976, Dr. Ole Hansen proposed that all CIBA GEIGY products should be boycotted in Sweden as the company continued to market or promote their products of Enterovioform and Mexaform in spite of conclusive evidence showing their relationship with SMON.

In 1977, the boycott started with doctors writing to the Swedish medical journals protesting against the continued sales of clioquinol. Thanks to the information obtained by a Swedish free-lance journalist from the CIBA GEIGY's internal documents.

On September 27, 1981 the Swedish newspapers published that for each individual drug, CIBA GEIGY lost 25% of their market in Sweden. CIBA GEIGY is said to have lost 75 million Swedish Kroner during the boycott years. In 1980, this was equivalent to the total turnover of CIBA GEIGY (Sweden).

The boycott by the Swedish doctors and the public was their way of contributing to the developing countries, fulfilling their responsibility towards all people in preventing drug suffering.

38 individuals afflicted with serious side effects by taking Mexaform, sued CIBA GEIGY for damages in Sweden. CIBA GEIGY and Draco agreed to pay 1.8 million Swedish Kroner as damages in an out of court settlement according to the Economic Times of the 14th April 1982.

JAPAN : About 10,000 persons are reported to be suffering from SMON in Japan. The number of suits in various parts of the country in September 1979, according to the Japan Times, was 5200.

It took more than 8 years and 4 months after the first SMON damage suit was brought against the State and three pharmaceutical companies (CIBA GEIGY - Japan Chemicals and Tanabe Selyakulo) for the Tokyo district court to reach two

decisions :-

1) Clioquinol causes SMON
2) CIBA GEIGY et al. were liable in failing to pass on information about the dangers of clioquinol.

Regarding the demand for appropriate instructions and a warning for doctors and patients, the company has argued :

"It is however not possible to achieve complete uniformity of the information for the doctors and patients, because in different countries there are different rules which are usually laid down by the local health authorities".

(Dr. J. Sobotkiewicz : Statement at Geneva Press Conference on SMON). Proc. of 28th April 1980 : p. 34.

(If there were no rules, more such drugs would be let loose on the public; and, in countries where the rules are lax, the people are obviously at the mercy of some unscrupulous drug industries who knowingly take full advantage of of these rules).

Some of the SMON victims who have won their cases are using part of their money to fight against needless drug induced suffering. According to Michiko Kinoshita, a SMON victim from Japan, in an interview with the New Internationalist, January 1981 :

"We want our fight against clioquinol in Japan to help secure assistance for SMON victims in other countries, just as thalidomide litigation in Europe and the USA helped gain assistance for thalidomide victims in Japan".

U.S.A. According to the National Drug Regulations, 1961, the use of clioquinol for amoebic dysentery is restricted. The maximum dose recommended is : 22.5 gm. for 10 days.

BANGLADESH The Bangladesh Government on June 12, 1982, acting on the advice of an Expert Committee, banned the manufacture, import, distribution and sale of 1707 drugs, which were considered irrational and harmful. Mexaform and Enterovioform and all products containing hydroxyquinolines have also been banned.

(A lesson India can follow from its small neighbour !)

ENGLAND In 1973, the UK saw no reason to restrict the sale of HOQ. However, in 1977, it was felt that oral clioquinol should be available only on prescription.

(Ref : Pharmaceutical Journal 1977 : 106,219)

In 1977, the Lancet had said :

"The time has come to halt free sales of clioquinol (i. e. enterovioform) and similar drugs for vague intestinal ailments and to demand good evidence before their use for other purposes is allowed to continue".

In London, in May 1978, the Sunday Times and BBC television covered in a programme the clioquinol dangers. This was following the briefing of a medical journalist and a T V producer by Dr. Ole Hansen.

Questions were raised in the parliament a few weeks later and just two months after the press and T V coverage, the Ministry of Health demanded that all bottles from pharmacies be withdrawn and the texts on the bottles and leaflets be altered. Even though these drugs are formally on prescription only, they have just disappeared from the market in England.

(The role of the press and Goverment Health Ministry needs to be noted and appreciated).

A point to note :
The Medical authorities in Britain had

said : "This (SMON) is no problem in Britain". Fortunately, in spite of them, these drugs have disappeared from the market in Britain.

INDIA According to the Hathi Committee, HOQ are supposed to be prescription drugs, but they can be obtained in any amount over the counter without prescription, without adequate warning. Even if the details of the warning were not written in such small print the English-knowing population being so small, the caution hardly succeeds in warning most of the consumers. Therefore, banning of dangerous drugs is the only solution in the absence of adequate control.

Our Plan of Action

1. Distribution of this briefing document amongst our drug core groups and discussion at the Drug Workshop.

2. Sending its summary to the Central and State Drug Controllers and Health Ministers.

3. Sending it to various medical and pharmacology heads for discussion and feedback.

4. Dissemination of this information via *Health For The Millions*, to our members, asking them not to prescribe this drug.

5. Dissemination to our journalists friends and consumer activists.

6. Demand for a warning which can be understood by consumers.

   Caution — The use of this drug may lead to blindness, loss of the function of your legs, loss of bladder control or constant pain in the legs. (Myelopathy, optic neuritis are meaningless for a consumer — as long as we can not ensure sales of potentially toxic drugs without a prescription, it becomes our responsibility to ensure adequate warning).

7. Demand that a cheaper alternative be made available.

8. Letters to MIMS, CIMS, IMA JOURNAL.

9. Try to get figures of SMON or suspected SMON cases from our colleagues in neurology or eye departments in the larger teaching colleges, PGI, NIMHANS, AIIMS.

10. Keep pressure on the Drug Controller to get Clioquinol banned and make alternatives easily available at low cost.

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N.H.Wadia, Department of Neurology, J.J. Hospital, Byculla.

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Japan Times Sunday(Sept. 16. 1979)

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11. Goodman Gillman

ALTERNATIVES

Nitronidazoles

like Metronidazole (INN)
Finidazole (INN)

PROS

- have amoebicidal action in the tissues as well as in the intestinal contents.

- they are fairly well tolerated by the majority, therefore Metronidazole can be used for amoebic dysentery as well as hepatic amoebiasis.

CONS

Occasional reports of neuropathy and mutogenic and carcinogenic potential in animal models (of uncertain relevance to man), has led to statutory requirements for warning labelling in the USA and India.

- Metronidazole is relatively costly.

Since Metronidazole is extensively absorbed in the small intestines and hence for greater and adequateaction in addition a lumenal amoebicide it should be routinely prescribed.

Diloxanide furoate

PROS

- is highly effective against nonsymptomatic carriers.

- in 95% cases eradication of organisms has been reported

- reqarding its use in acute amoebic dysentery divergent results have been obtained – concurrent use of tissue amoebicide whenever possible is recommended.

Paromomycine Aminoglycoside

Antibiotic-Is effective both for symptom less causes and acute amoebic dysentery.

CONS

High cost

Troublesome diarrhoea

Carbasone arsenical and Glycobiarsol gave unimpressive performance-isolated fatalities attributed to carbasone.

- occasionally - evidence of cumulative toxicity.

- the choice of lumenal amoebocide should be based on its effectiveness.

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DRUGS CONTAINING HYDROXYQUINOLINE

BRAND	DRUG HOUSE
Ambactin-4	B C P W
Amoebindon	Indon
Aldiamycin	Alkem
Aldiamycin Suspension	Alkem
Alliquin	Standard Pharmaceuticals
Amebys	Napha
Ambilan	Swastlk Pharmaceuticals
Amoechin	Universal Drug House
Antidar	Dextromed
Bioxyl	Bio-Drug
Chlorambin	Anglo-French

Colon	Emsons
Davoquin	Albert David
Dequinol	Dey's Medical Stores
Dependal	S K & F
Dysenchlor	S G Chemicals
Digichlor	T H P
Diodoquin	Searle
Di-Iodohydroxyquin	Semit
Di-Iodohydraxyquinoline	T H P
Di-Iodohydraxyquinoline	Fairdeal
Di-Iodohydraxyquinoline	Usan
Di-Iodohydraxyquinoline	Baropharn
Dinochlor	Bengal Immunity
Dinoquin	Bengal Immunity
Diorcin	Cos Pharma
Dystrindon	Indon
Dysental	Quality Pharmaceuticals
Dysentol	Bronkal Pvt Ltd
Dysentriad	GDA Chemicals
Enteroton	I N D C
Entro Iodochlor	Bombay Tablet
Embaquin	M & B
Entrokin	Bengal Chemicals
Entroquinol	Indo-Pharma Lab
Entero-Vioform	Ciba-Geigy
Intestopan-In	Sandoz
Faircolin	Fairdeal
Fairdiquin	Fairdeal
Floraquin	Searle
Furoquinol	Chogule
Histoquin	Zandu
Idosulpain	Indo Pharma
Indoquin	Indoco
Intestopan-Q	Sandoz
Intestopan Suspension	Sandoz
Labrody	Labros Chemicals
Lumigyl Caplets	Ethico
Mebinol Complex	MAC Labs
Mexaform	Ciba-Geigy
Neoquin	Sunways
Moebagym	Ebers
Phenipan	Sandoz
Quiniform	Albert David
Quinogel Compound	Acilla
Stadmed Entrozyme	Stamed
Sulfaquinol	Comteck
Sulphaquino-Bael	Standar Pharmaceuticals
Sulphazyme	INDC
Uni-Dys	Unichem
Yodchin Sulpha	Duphar, Navaratna

Courtesy :- *V.H.A.I., New Delhi.*

BANNING OF DRUGS

The law, the persons and mechanisms involved in the banning of drugs are being reviewed in brief.

LAW - According to the Drugs and Cosmetics Act, 1977 under the section 'Prohibition of manufacture and sale of certain drugs' –

Manufacture for sale of

1. a. any drug not of standard quality

   b. any misbranded or adulterated drug

   c. any patent or proprietry medicine which does not display the formula and list of ingredients in the prescribed and readable manner.

   d. any drug claiming to prevent any such disease or claiming to have any other than prescribed effect

2. Any drug which has been imported or manufactured in contravention of any of the provisions or rules of this act.

3. Manufacture for sale of any drug not in accordance with the condition of a licence issued for such purpose.

In May 1982, it was announced in the Lok Sabha that the Drugs & Cosmetics Act is to be amended soon to provide stringent punishment to manufacturers of spurious drugs. Imprisonment for 5 years and a fine of Rs. 10,000.00 if consumption of such drugs results in death or grievous hurt to patients. Similar punishments for offences in the indigenous drugs is also proposed to be enhanced. Manufacture and sale of drugs without valid licence – imprisonment 1 – 3 years and a fine of Rs. 5000.00. Other points are definition of spurious drugs, more power to drug inspectors and central drug controllers, etc..

Drug Control Organizations / Bodies

1. *The Drug Controller of India (DCI) at the center and the Food and Drug Administration at the State level (State Drug Controller – SDC) their prime role is to screen drugs* before they can be marketed in the country. They assess their utility and clearly outline their side effects and ill effects.

2. Two bodies are formed to go into the technicalities of the issue and advice the government.

   a. *The Drugs Technical Advisory Board (DTAB)* 18 member board to *advice the center and state on administration of the Drugs Act* and to carry out other functions assigned to it by the Act

   b. *The Drugs Consultative Committes (DCC)* – advisory committee to center and state and DTAB on many matter tending to *secure uniformity throughout India in the administration of this Act*.

3. Drug Analysis Labs

   a. except Maharashtra, Gujarat, Tamil Nadu, Kerala and Karnataka no other state has streamlined its drug control machinery

   b. the central Indian Pharmacopeia lab in Ghaziabad and the Central Drug Lab in Calcutta are the two final analysis labs at central level. They act as the Government analyst for Andhra Pradesh, Bihar, Delhi, Goa, Tripura, Orissa and Rajasthan

   c. in Delhi there are four private testing labs approved by the

Government :

i) Sri Ram Institute of Industrial Research
ii) Analytical Testing Services
iii) Reliable Test Laboratory
iv) Industrial Research Laboratory

4. Apart from these organizations there are many ministries and departments involved in the drug scene in India and the D C I will take the final decision in any matter after consulting these ministries etc.

a. *The ministty of Petroleum and Chemicals imports, exports and distributes drugs* all over India and also *fixes prices* for the different categories of drugs

b. *Finance Ministry issues licences* for procurement, stocking and sale of drugs. Licence for labelling, bottling and packing is given by yet another department

c. t h e *parliamentary consultative committee* attached to the Health Ministry helps in *calling the attention* of Drug Control authorities to the *harmful effects of drugs*

d. *the Central Drug Standard Control Organization* helps in the *quality control of imported drugs*

In June 1982, *the Drug task force* was announced to go into the problem of spurious and sub-standard drugs. It will have the Additional Health Secretary and six other members

i) adequacy of drug control at centre/state and measures to strengthen it

ii) need for increasing the drug testing facilities at center/state

iii) need for setting up Intelligence Cells in the states and central drug control organization to combat the problem of spurious and sub-standard drugs

iv) changes needed in procedures relating to control over licencing, manufacture and sale of drugs under the Drugs Act.

List of Drugs Banned

1. 5.12.81 – Out of the 18 drugs recommended for removal by WHO, 6 were not approved in India, action has been taken to withdraw 7, and 5 have been allowed to remain on the market with a cautionary statement on the labelling. They are nitrofuran compounds, phenaformin, oxyquinoline derivative, higher does lynoestrenol products and pregnancy tests.

2. 28.1.82 – The Government banned manufacture of *Pencillin Eye ointment* because it induced sensitization in the patients.

3. 1.5.82 – manufacture of *paediatric tetracycline drops* had been banned. But no date is given for stopping marketing. 'Phased discontinuation, was not in practice at that time. But now, date will be announced soon.

4. 4.5.82 – The Government decided to weed out *18 drug formulation* as they were considered harmful, (see list attached). The DCC appointed a sub-committee to examine 32 groups of fixed dose combination. Their recommendations were again considered with DCC, which recommended 23 categories could be weeded out. The matter went to DTAB and it finally recommended weeding out 18 drug combinations. Neoessary action has to be taken by State Drug Controllers.

5. 19.6.82 – Sequel to V C Sane panel report – the Government decided to withdraw *350 unnecessary drug*

formulations. These are the products (brand names) of the 18 weeded out drug formulations. These products were randomly selected from the Pharmaceutical Guide. Many more will follow. The firms were asked to stop production by the end of September 30, 1982 and marketing and sale by March 31, 1983. This is called *'Phased discontinuation'*. The purpose is to give a time limit to firms who may have already purchased the bulk drug for manufacturing the formulations. Out of the 350 brands – 44 are marketed by foreign drug companies, 8 by Indian public sector and the rest by private sectors.

6. 30.5.82 – Government banned the drug *Amidopyrine* and also its formulations. The DCI issued orders to stop manufacturing by July 1, 1982 and sale by October 31, 1982.

7. 30.6.82 — the government decided to put a ban to all *pregnancy testing medicines*— fixed dose combinations of oestrogen / progesterone. The stipulated cut off date for the manufacture is December 31, 1982 and sale on June 30, 1983. Many concerned health groups are demanding an immediate ban.

Harmful Drugs Not Yet Banned

1. *Anabolic Steriods* – the Drug Controller of India said that the Government is looking into some of the Anabolic Steriods — their hazards etc. The matter is under consideration. Ciba-geigy has withdrawn Dianabol.

2. *Streptomycin and pencillin combinations* – the DTAB felt that it is necessary for treatment in mixed infections and its a cheap drug. But TB authorities strongly demand a ban on it.

3. *Analgin* – the Drug Controller of India said Hoechst, University of Boston and West Germany are doing the toxicity study of analgin individually. The Government is awaiting the result and then action will be taken. The DCI is interested to know if a similar study will be conducted by voluntary organizations; so that a decision could be taken after considering both the studies.

4. *Clinoquinol* – The DCI said that 'it should not be banned because it is the best and cheap drug for dysentery in India. More people die of starvation here than of SMON. The conditions of the hospitals and other factors have to be considered not only the drug.'

ACTUAL SITUATION – with all the acts, boards and committees what's actually happening is as follows :

1. Presently over *30,000 drug formulation* are marketed by *5000 drug companies* in India. Out of which *3000 are small scale firms* – these firms products are relatively cheaper but their quality control is not up to the mark.

2. There are only *600 drug inspectors* in India. They can hardly keep a close watch on thousands of manufacturing and innumerable retailers spread all over the country.

3. *Drugs banned in the West* or used under severe restrictions always *continue to be liberally used in India.* Eg. anabolic steroids, analgin, etc.

4. It takes years to decide on an issue and decades to implement the decisions.

5. The DCI said that the *centers DC office* is just a *policy making body* for uniform policies throughout India. While the *State Drugs Controllers have more powers to implement and to take decisions, etc.* But the *Delhi*

(State) Administration Drug Controllers office gives another picture. They said that the State Drug office have actually no powers but just do whatever the center says, etc.

6. There is a lot of controversy over the *drug* price control order. For 15–18 essential drugs there is no excise duty. Previously the Govt. charged $2\frac{1}{2}\%$. The rest of the drugs have *heavy duty like customs duty (18%), central excise duty (12%), central sales tax, state sales tax etc.* The drug companies are against this heavy taxation. But the Finance Ministry is in a fix because the Budget depends on the 100 crore contribution from drug industry through its taxes ! !

LOOPHOLES IN THE LAW – the manufacturers have simple ways of defeating the provisions :

1. In connivance with or by *misrepresenting the DC* of the state and secure a licence.

2. *Copying* an allopathic name, design, printing and packing but making the contents ayurvedic, e.g. Crocin as 'Erocin'. Since the definition of misbranded drugs does not apply to ayurvedic products no law can touch the imitators for the violation of the Act. The Delhi Administration Drug Controller's office has a special cell for receiving complaints regarding spurious drugs (Phone No. 226018)

3. Chemists selling ayurvedic drugs do not require a selling licence.

4. *Penalty is not particularly severe.* They usually get away with minimal sentences.

Problems in the D C Organisation

1. The tragedy with the working and operations of *DCO and PDA* is that they are *given extremely low priority by the central and state Government.* Lack of funds, manpower, facilities add to the poor condition of these organizations there are no specialists in pharmacology and even the concerned persons are not well versed with the current and crucial information on drugs.

2. *F D A* – is a small office manned by a handful of men. It has *not been able to keepchemists under control.* It rarely prosecutes erring chemists.

3. Because of lack funds and machinery the DCI asks the drug manufacturers to carry out tests on his own at Government and Municipal hospitals under the supervision of DCI officials. This system works totally in favour of the manufacturers. The *common methods of manipulation include altering statistical data, overlooking* relatively minor side effects etc.

4. *Too many varied ministries and organizations are involved in the drug scene in India.* When the DCI was approached to enquire whether the whole issue of drugs could be taken up by the Health Ministry, he said 'drugs are chemicals. Chemicals could be used as drugs, dyes, fertilizers, etc. Technically it cannot come under Health Ministry. Imports, exports licencing etc, are involved and so a seperate ministry of chemicals and fertilizer was opened mainly to look after this area.'

5. *Drugs could not be banned easily in India as we have a planned economy.* There is control and restrictions in each and every matter. But in USA there is free economy and no control over prices and no licences are issued. So it is easier for USA to ban drugs.

Suggestions for Improvement

1. Amendmends in the Drugs and

Cosmetic Act.

2. To *bifurcate* the food and drug testing agencies with seperate head for each, like in Maharashtra.

3. To *increase the number of drug inspectors* in India.

4. To *clearly define the role, function and powers of DCI and State Drug Controllers.*

5. To *include atleast one or two members from the voluntary sector in the DCC and DTAB.* At present the members are only state drug controllers.

6. To see that the essential drugs are available easily and cheaply.

7. To carefully screen the imported drugs and *not to introduce the drugs when they are banned abroad.*

8. *To start the drug control machinery* with drug testing labs *in each State*

9. To formulate *rules, regulations and price control for indigenous manufacturers.*

10. To formulate a *code for drugs* (like IFPMA)

So, by streamlining the drug administration and management in India many improvements could be done in this area.

Courtesy : *V.H A.I., New Delhi*

INTERNATIONAL FEDERATION OF PHARMACEUTICAL MANUFACTURERS ASSOCIATIONS (IFPMA)

CODE OF PHARMACEUTICAL MARKETING PRACTICES

Preamble

The Statute of the Federation article 3 states that one of the objects of the Federation is "to promote and support continuous development throughout the pharmaceutical industry of ethical principles and practices voluntary agreed on and to coordinate the efforts of its members towards the realization of the above objects."

It is believed that in keeping with the pharmaceutical industry's international responsibilities, the members of the Federation will be prepared to accept certain obligations, insofar as their marketing practices are concerned, and to ensure respect for them.

IFPMA recommends a Code of Marketing Practices to its member associations, recognizing the difficulty of setting out a simple Code which will be applicable in all parts of the world. It seems clear that national and regional conditions and legal restrictions will continue to vary to such an extent as to make a simple world Code impractical. Nevertheless, the Federation believes that it has a duty to encourage its member associations to either introduce such Codes of Practices or where such Codes already exist, to continually re-examine and where necessary revise them so that a voluntary system based on such a Code keeps pace with modern medical knowledge and changing health services and conditions.

It is recognized that many individual member associations of IFPMA have laid down their own Codes of Marketing Practices and this recommended Code is not intended to replace similar Codes or instruments already in force by members of the Federation. The following voluntary Code is therefore put forward as a model for IFPMA's member associations.

A Code of Marketing Practices of this sort should be the responsibility of member associations who should also provide guidance to their members on matters of compliance and interpretation.

Obligations of the industry

The obligations of the industry may be identified as follows :

The pharmaceutical industry, conscious of its special position arising from its involvement in public health, and justifiably eager to fulfil its obligations in a free and fully responsible manner, undertakes :

- to ensure that all products it makes available for prescription purposes to the public are backed by the fullest technological service and have full regard to the needs of public health;
- to produce pharmaceutical products under adequate procedures and strict quality assurance;
- to base the claims for substances and formulations on valid scientific evidence, thus determining the therapeutic indications and conditions of use;
- to provide scientific information with objectivity and good taste, with scrupulous regard for truth, and with clear statements with respect to indications, contra-indications, tolerance and toxicity;
- to use complete candour in dealings with public health officials, health care professionals and the public.

Suggested Code of Marketing Practices

We hereby declare our intention to voluntarily conform to the following Code

of Marketing Practices :

I. *General Principles*

1. The term "pharmaceutical product", in this concept means any pharmaceutical or biological product intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease in humans, or to affect the structure or any function of the human body, which is promoted and advertised to the medical profession rather than directly to the lay public.

2. Information on pharmaceutical products should be accurate, fair and objective and presented in such a way as to conform not only to legal requirements but also to ethical standards and to standards of good taste.

3. Information should be based on an up to date evaluation of all the available scientific evidence, and should reflect this evidence clearly.

4. No public communication shall be made with the intent of promoting a pharmaceutical product as safe and effective for any use before the required approval of the pharmaceutical product for marketing for such use is obtained. However, this provision is not intended to abridge the right of the scientific community and the public to be fully informed concerning scientific and medical progress. It is not intended to restrict a full and proper exchange of scientific information concerning a pharmaceutical product, including appropriate dissemination of investigational findings in scientific or lay communications media, nor to restrict public disclosure to stockholders and others concerning any pharmaceutical product as may be required or desirable under law, rule or regulation.

5. Statements in promotional communications should be based upon substantial scientific evidence or other responsible medical opinion. Claims should not be stronger than such evidence warrants. Every effort should be made to avoid ambiguity.

6. Particular care should be taken that essential information as to pharmaceutical products' safety, contraindications and side effects or toxic hazards is appropriately and consistently communicated subject to the legal, regulatory and medical practices of each nation. The word "safe" must not be used without qualification.

7. Promotional communications should have medical clearance, or where appropriate, clearance by the responsible pharmacist, before their release.

II. *Medical Representative*

Medical representatives must be adequately trained and possess sufficient medical and technical knowledge to present information on their company's products in an accurate and responsible manner.

III. Symposia, congresses and other means of verbal communication.

Symposia, congresses and the like are indispensable for the dissemination of knowledge and experience. Scientific objectives should be the principal focus in arranging such meetings, and entertainment and other hospitality shall not be inconsistent with such objectives.

IV. *Printed Promotional Material*

Scientific and technical information shall fully disclose the properties of the pharmaceutical product as approved in the country in question based on current scientific knowledge including:

— The active ingredients, using the approved names where such names

exist.

— At least one approved indication for use together with the dosage and method of use.

— A succinct statement of the side-effects, precautions and contraindications.

Except for pharmaceutical products where use entails specific precautionary measures, reminders need not necessarily contain all the above information providing that a form of words is used which indicates clearly that further information is available on request.

Promotional material, such as mailings and medical journal advertisements, must not be designed to disguise their real nature and the frequency and volume of such mailings should not be offensive to the health care professionals.

V. *Samples*

Samples may be supplied to the medical and allied professions to familiarize them with the products, to enable them to gain experience with the product in their practice, or upon request.

Courtesy : *V.H.A.I., New Delhi*

ARE HORMONAL PREGNANCY TESTS SAFE ?

Widespread indiscriminate misuse of Oestrogen-Progesterone combination drugs in pregnant women is cause for grave concern.

This is inspite of the fact that the scientific group of the WHO on "THE EFFECT OF FEMALE SEX HORMONES ON FOETAL DEVELOPMENT AND INFANT HEALTH" in its report 'WHO TECHNICAL REPORT SERIES 657, 1981' have recommended that *"these tests should no longer be done."*

The approved pharmacology text book for medical schools, Goodman and Gilman says "PREGNANT PATIENTS SHOULD NOT BE GIVEN OESTROGENS, PARTICULARLY DURING THE FIRST TRIMESTER - a time when the foetal reproductive tract is developing and may be influenced by exogenous oestrogens. For the diagnosis of pregnancy, immune-assay of urinary chorionic gonadotropin, which is increased very early during the first trimester of pregnancy is a relatively simple technique and is preferred."

"Hormonal tests for pregnancy are not reliable. THE TEST IS FALSE POSITIVE IN ONE OUT OF FIVE WOMEN : THERE IS ALSO AN INCREASED RISK OF FOETAL ABNORMALITIES." (D. Vengada Salam et al: International Journal of Gynaecology and Obstetrics.) 14:348-353, 1976.

In a study with 149 abnormal babies (70 with malformations of the CNS, 9 with reduction deformities of the limbs, 13 with congenital disease, 11 with Downs Syndrome, and 46 with other malformations) with 149 controls. Of this, a total of 23 mothers of abnormal babies had been exposed during the first trimester of pregnancy to drugs containing hormones compared with only eight of the control mothers. One of the 23 had also taken an oral contraceptive and tablets of nor-ethisterone. This evidence supports the recommendation that "THERE IS LITTLE JUSTIFICATION FOR THE CONTINUED USE OF WITHDRAWAL TYPE OF PREGNANCY TESTS WHEN ALTERNATIVE METHODS ARE AVAILABLE." (Excerpt from a letter written in the British Medical Journal, 26th April 1975, page 192, by G. Green Benz and W. H. H. Inman of 'Committee on Safety of Medicines,' London and Josephine A. C. Weatherall and A. M. Adelstein of the 'Office of Population and Census and Survey,' London.)

"In any case, as we have earlier stated, and as Janerich and his co-workers have concluded," IT IS PRUDENT TO DISCONTINUE THE USE OF HORMONAL PREGNANCY TESTS." (Editorial : 'The New England Journal of Medicine' Volume 291, No. 14, Page 731)

"Contrary to previous assumptions new data suggest that the administration of hormone will not hasten and may even delay the onset of menstrual bleeding. This lack of efficacy together with some evidence of 'increased incidence of congenital malformations' associated with the administration of hormones in early pregnancy suggests that *hormonal withdrawal test should be abandoned."* (Integrated Obstetrics and Gynaecology for Post Graduates by Dewhurst.)

"Moreover, currently there is the fear that progestons are potential teratogens. While the evidence to support such a conclusion is not yet definitive, nonetheless, considering the lack of utility of this procedure, PROGESTIN INDUCED WITHDRAWAL MENSES AS A TEST OF PREGNANCY CANNOT BE RECOMMENDED." (Williams Obstetrics, 16th edition, 1980.)

"PREGNANT PATIENTS SHOULD NOT BE GIVEN ESTROGENS,' PARTICULARLY DURING THE FIRST TRIMESTER – a time when the foetal reproductive tract is developing and may be influenced by exogenous estrogens." (Progesterone on Threatened Abortion : Goodman Gilman, 1980, Pages

1439-1440).

The above extracts from 'medical literature' are just to give added evidence to the fact that these pregnancy tests are no longer considered safe. In view of the dangers associated with their use, prescribing them is not merely UNETHICAL: it is almost CRIMINAL.

Even where RELIABILITY AS A PREGNANCY TEST is concerned hormonal preparations like EP Forte have been found to have 18.91% FALSE POSITIVES according to a study conducted by D. Vengada Salam et al (International Journal of Gynaecology and Obstetrics 14: 348-352, 1976).

The FOETAL ABNORMALITIES linked with the use of hormones during early pregnancy are limb reduction defects, congenital defects of the great vessels, the VACTERL association and di George Syndrome (Thymus Parathyroid aplasia) according to observations in the study done by Levy Cohen & Frazer and the study done by Nora and Nora.

'According to Isabel Gel in 'Nature': Volume 240, November 24, 1972, "The pregnancy test works by altering the maternal equilibrium and because the hormonal changes produced by the tablets are sufficiently effective to disturb a non-pregnant uterus, there is a strong possibility that the pregnancy case will be affected as well."

Probably on this consideration hormonal pregnancy tests are frequently used with the very intention of inducing abortion apparently successfully in susceptible individuals. The Royal College of General Practitioners Survey into the outcome of pregnancy found, a 10% ABORTION RATE after primodes administration. Brotherton & Craft reported an incidence of 7.6% *SPONTANEOUS ABORTION* following the use of hormonal pregnancy tests. What about women who do not wish to risk such a thing — is exposing them to it justified ?

"It is possible that in less sensitive cases the relatively large dose of hormone in pregnancy test tablets may interfere with the foeto-placental unit, by upsetting the hormonal balance of the mother, the foetus or the interaction between them. This may not interrupt pregnancy but may affect FOETAL DEVELOPMENT."

Another cause of concern is the EXPOSURE OF WOMEN TO HORMONAL PREPARATIONS FOR VARIOUS REASONS, from contraception to pregnancy tests, for alleged maintaining pregnancy in cases of threatened and habitual abortion, for irregular periods, for functional uterine haemorrhage, etc.

This takes on a serious magnitude since such preparations can be prescribed by the qualified as well as the unqualified health personnel. An adequately trained and supervised knowledgeable and concerned health personnel not holding a degree is not half as dangerous as a smooth-talking profit oriented medical person even if he or she has a string of qualifications attached. This is so because no one dares to question the latter's wisdom, and worse still is the fact that the latter set the trends - efficiency and concern for the patients are not always associated with popularity of the medical professionals.

These preparations can be bought over the counter EVEN WITHOUT PRESCRIPTION as was our experience, there is no warning with these preparations (E.P. Forte tablets and injections). Even on specifically asking for the *Literature* we were told that the *literature* is given only to the prescribing doctors. This of course, leads one to believe that the prescribing doctors would READ THIS LITERATURE and communicate this information to the woman being prescribed this diagnostic test. One would expect the CHEMIST selling the drug specially when it is without a prescription to communicate this information. Very obviously THIS LITERATURE IS EITHER NOT READ OR TOTALLY IGNORED. So even if the drug companies swear by this *literature* — ITS VALUE AS AN EFFECTIVE

MODE OF COMMUNICATIONS IS VERY DOUBTFUL. Even if this often microscopically written drug related information is made available it is often in a LANGUAGE NOT EASILY UNDERSTOOD BY THE CONSUMER – eg. any relationship of 'secondary ammenorrhoea' with pregnancy is not at all clear. The most important fact still remains HOW MANY WOMEN BEING PRESCRIBED THIS DRUG CAN READ AND THAT TOO IN ENGLISH and in a PRINT-SIZE WHICH OFTEN REQUIRES EITHER PERFECT EYESIGHT OR THE USE OF A MAGNIFYING GLASS ?

The THALIDOMIDE DISASTER has not yet been forgotten where this popular drug given to pregnant women caused abnormalities of the limbs in more than 6,000 children in West Germany alone. This drug was sold under *90 brands* and even if information about the dangers of Thalidomide were made known, how many women would realise that the brand drug they were taking contained Thalidomide ? How many even know that the tablets and injections they are taking are hormones ?

How many more allegedly "statistically significant tragedies" do we need to avoid dangerous preparations and opt for less toxic alternatives ?

In India where women are relegated by society to second class citizenship, where even bearing a normal female child by her is looked upon as her failure – knowingly exposing her to the dangers of bringing an abnormal malformed child into the world is CRIMINAL.

Today the evidence about the dangers of pregnancy tests are well documented and the earlier agreement of 'statistically not significant' does not hold good.

The recent issues of commonly used referral sources of information by prescribers, the MIMS (Monthly Index of Monthly Specialities) and the CIMS (Current Index of Monthly Specialities) have added pregnancy in the contra-indications. This is not so for all the preparations. For some preparations it is written, 'See Literature'. How many prescribers take the trouble to dig out this literature and read it, is anybody's guess. *Some preparations are still indicated for pregnancy in the MIMS.*

Since this warning about not using it in pregnancy has been added in only the most recent issues of MIMS and CIMS, one wonders, in how many readers' minds has this change registered. Do the drug companies supplying these preparations to the chemists and the prescribers have a responsibility of categorically warning them of this *change ?* If it is their responsibility who ensures that UNBIASED INFORMATION is given to the chemist, the doctor and the consumer ?

Who ensures that some form of regulatory measures for the prescribers are formulated to prescribe and control malpractice ? This single action may do a lot in ensuring ethical medical practice, but it may also become something of an eye-wash, leading to undue harassment of the innocent and allowing the guilty to tip their way out. Any worthwhile control has to come from the AWARE PUBLIC which keeps itself well informed to avoid exploitation of any form, done knowingly or unknowingly.

> IT IS THE UNDENIABLE RIGHT OF A CONSUMER. TO BE TOLD ABOUT THE HAZARDS OF SOME OF THE KNOWN PROBLEM DRUGS – MORE SO IT IS THE RIGHT OF A PREGNANT WOMAN TO KNOW THE SIDE EFFECTS OF ANY DRUG PRESCRIBED FOR HER.

For this, what we recommend is :

PRINTING OF THE CAUTION AND WARNING ON THE DRUG PACKET ITSELF, warning against its use as a PREGNANCY TEST OR in PREGNANCY.

There is a need to develop ALTERNATIVE CHEAP NON-HAZARDOUS DIAGNOSTIC TESTS FOR EARLY PREGNANCY. As a

collosal amount is spent on contraceptive research, some amount could be definitely allotted for simple early pregnancy tests.

Since delay in detection of pregnancy leads to problems as in the case of a woman wanting termination of pregnancy — the fact that six lakh Indian women die due to criminal abortion has its own tragic story to tell. Early detection is associated with simple and safer termination procedures.

This diagnostic pregnancy test is RECOMMENDED FOR ONLY THOSE WOMEN WHO WISH TO TERMINATE THEIR PREGNANCY, IF FOUND PREGNANT, according to medical literature. This, of course, is not to be misinterpreted as a recommendation for MTP (medical termination of pregnancy). With adequate precautionary measures an unwanted pregnancy should not occur — if it does, it is the woman's right to choose how to progress with it. It is the responsibility of the physician and the pharmaceuticals to give all the appropriate information about the dangers of all drugs prescribed.

It is the role of women's groups, consumer associations and socially conscious individuals to disseminate and share relevant information. If the health personnel could have done this, so many of the problems would have probably not existed in the first place.

The idea of our involvement with all this is because of our concern for women who are passive recipients of many potentially hazardous drugs, when low cost, less hazardous alternatives may exist. All those concerned have no choice but to join in. Any additional information can be obtained from VHAI. If we dont have it we would dig it up for those involved in issues of women and health.

Dr. Sathyamala

Dr. Mira Shiva

Courtesy : *V.H.A.I., New Delhi*

LOW COST DRUGS AND RATIONAL DRUG THERAPY
INTERNATIONAL CODES AND YOU!

Last year the WHO was instrumental in passing an International Code of Conduct of Marketing Practice of Baby foods.

This not only focussed the attention of the public, the health professionals on the baby food issue, but placed the concept of breast feeding from a 'rustic, old fashioned practice' to scientifically sound and recommended one. What this will do to the commercial interests of the milk food industry is anybody's guess? It is up to the aware public, the consumer associations, the journalists to ensure that the code of conduct of which India was a signatury — is firmly adhered to.

The contents of this code are being circulated for awareness and action of the health personnel and the public.

Along with it is a copy of the International Code of Pharmaceutical Marketing Practice, proposed by IFPMA (International Federation of Pharmaceutical Manufacturers Associations).

A copy of this provisional code was given to the participants of our Drug Workshop at Poona, for discussion and comments.

The code is being circulated along with extracts from the discussion document prepared by Health Action International on the code.

You are requested to read it carefully, share it with your colleagues and pass it on. Your comments and suggestions regarding the international code of pharmaceutical marketing practice are requested.

You are requested also to bring to our notice, cases of malpractice by drug companies which may be, by way of misinformation, selling of spurious drugs, unethical marketing practices, commissions for prescriptions, cut backs etc. Your participation is not only requested but is NEEDED for us and other groups and organisations to take any legal action, for malpractices to be curtailed before it is too late.

What is IFPMA?

IFPMA is an International Federation of Pharmaceutical Manufacturers Association, a Zurieh-based trade organisation, set up and supported by a number of national associations of manufacturers of prescription drugs. Altogether there are 30 affiliated through the Latin American Association of the Pharmaceutical Industry.

Why the IFPMA Code was introduced and what it aims to be?

"The Paris-based International Chamber of Commerce has published codes of advertising and marketing practice — which are meant to apply to business of all kinds. However, the IFPMA Code (which makes no reference to the requirements of the International Chamber of Commerce) is believed to be the first ever attempt to introduce an international code of marketing practice for pharmaceutical companies.

The preamble of the IFPMA Code (Appendix) explains how its terms of reference extend to the drawing up of a voluntary code of practice. Though the IFPMA does not state why it decided to introduce a code at this time, the following factors would certainly have been important :

1. There has been considerable criticism of the activity of the international pharmaceutical industry, and it appears to be increasing. The industry has given little evidence to suggest that it accepts such criticism — but would certainly be aware, at least, that health - care professionals increasingly find it legitimate and

to the point. The relative success of the campaign coordinated by the International Baby Food Action Network (IBFAN) has demonstrated the potential for international action by media, consumer, public interest and development and health action groups-particularly where developing countries are concerned.

2. The need to avoid further statutory regulation of the industry at either national or international level. The indications are that the IFPMA proposed its Code in response to the threat of a move by the World Health Assembly to work towards the setting up of a formal international code of pharmaceutical marketing practice. In the event, the threat did not materialise at the Summer 1981, World Health Assembly—but there remains the possibility of future initiative, if not through the World Health Organisation or UNCTAD, then possibly through the UN Centre on Transnational Corporations.

3. The credibility of the industry - now clearly under threat - is a vital commercial asset. Lack of confidence in the drug industry by those who regulate, prescribe or use pharmaceutical products could be commercially disastrous. It is clearly critical that the industry generally, as well as individual drug companies, is trusted and seen to 'care'.

The IFPMA has responded to these (and perhaps other) imperatives by first, issuing a statement of 'the obligations' of the pharmaceutical industry; and secondly, by suggesting a number of 'general principles' by which these obligations might be fulfilled.

It is important to recognise that, in doing so, the IFPMA is not trying to introduce its own 'simple world code'. The IFPMA specifically says this would be 'impractical' because of differences in local conditions. All IFPMA is trying to do with its Code is 'to encourage' national member organisations either to introduce or to revise their own voluntary codes."

What stage of implementation is the Code in ?

"The document has not yet been formally adopted or published : it is reproduced here in the form in which it was circulated for comment to IFPMA member associations, in March 1981. Since then, the Code has been agreed by the IFPMA Council and by the end of June 1981, it had been approved also by all of the major associations within IFPMA."

What is the purpose of the discussion document circulated by HAI ?

"The purpose of this paper is :

1. to draw attention to the existence and provisions of the IFPMA Code;
2. to discuss briefly its significance in relation to controls that are needed and which might be applied; and
3. to suggest options for action by HAI participating groups."

According to the discussion document, what are the three essential ingredients of any code of practice omitted in this IFPMA's Code?

1. Need for interpretation

Reference to the need to ensure that the industry makes products which have full regard to the needs of public health - appears a statement so vague that it is hard to accept it as anything much more than an advertising or public relations slogan.

2. Need for monitoring

The question raised is 'what assurance is there, that the code will be adhered to?' Is the Code to operate on the basis of a complaints procedure? The mechanism for complaints handling and monitoring, which are fundamental to a code have not been referred to.

3. Need for enforcement

What happens if the Code is violated?

- — who judges? industry (through its association or otherwise) or truly independent bodies.
- — whether enforcement decisions are published - or this is kept a secret? Could it be possible to establish, on the basis of past decisions, what practices are acceptable or unacceptable? And what is the record of individual companies where complying with the Code is concerned.
- — what actions would be applied if companies break the provisions of the Code?
- — what incentive is there for firms to observe the requirement of the Code?

What are the implications and significance of this for the HAI groups?

This is useful to refer to the obligations of the industry identified by IFPMA;

Individual groups may think alternative or additional requirments which might be needed to control abuse in pharmaceutical marketing, and to consider how such requirments might effectively be enforced at both national and international level;
Groups might also wish to collect examples of apparent malpractice;

Collectively, groups may find it useful to exchange infomation or the design and enforcement of standards under different voluntary (self regulatory) systems operating in their countries. Groups might also wish to campare and pool the evidence they obtain about apparent malpractice and to publish and publicise this evidence both locally and internationally through HAI.

HAI would like to know whether it should press for introduction of an international code of pharmaceutical marketing practice which has "teeth," and which can reasonably be expected to work through WHO/UNCTAD and national governments.

YOUR RESPONSE IS NEEDED URGENTLY

Courtesy: V.H.A.I.

WHY NOT TO PRESCRIBE ANABOLIC STEROIDS

The unquestionable, unshakeable faith in tonics and vitamins of the majority of us - Indians is due primarily to the excellent marketing strategies of the drug companies, and the compliance of the health professionals and the consumers.

The uselessness of tonics and vitamins is abundantly clear to those who care to question their rationality. Where anabolic steroids are concerned, the potential hazards associated with it sintake make it a doubly black-listed product.

Anabolic Hormones - "most of them are weak versions of male sex hormones and were synthesised and introduced into medicine as agents to speed the transformation of foodstuffs into body tissues. They were originally promoted-and some still are - as drugs that could stimulate the appetite, step up body weight, strengthen bones, increase athletic ability, control a variety of emaciating diseases and in the recovery from surgery, infections, burns, fractures and severe traumatic injuries"

Ref : Prescription for Death" p.67
Milton silverman.

Accepted Indications

Based on objective evidence anabolic hormones are accepted for use in :

- certain kinds of (aplastic) anaemias.
- inoperable breast cancer.
- prevention and treatment of osteoporosis
- bone softening as seen in post-menopause of women
- senile patients.

But used as an adjunct and not as primary therapy-diet, calcium balance, physiotherapy and good general health promoting measures need equal or greater consideration.

Toxicity

In large quantities, they may cause

In Women

— masculinization	irreversible
— baldness	
— deeping of the voice	virilization
— hirsutism	
— menstrual irregularities	

Adverse effect on liver - jaundice, liver tumors.

May cause sodium retention - leading to edemia and heart failure. Can cause problems in cardiac, renal or hepatic diseases and increased or decreased libido.

In young children

— Early closure of epiphyses in the bones resulting in stunted growth.

Boys

— precocious sexual development.

Young girls

— they can produce enlargment of the clitoris or the development of false penis.

— Alteration in glucose tolerance test, thyroid function test. Elec trolytes — sodium chloride water phosphates, calcium.

Liver Function Test : Serum cholesterol, suppression of clotting factors, II, V, VII & X

/(Editorial: Pune Journal of Ongoing Education)

How adequately these warnings are given to the prescribing doctor by the drug company or to the consumer by the doctor —is well known !!

When the actual problem is lack of food, the solution is not tonics or anabolic steroids. When the desired action should be to look deeply into the causes of malnutrition-our major health problem - a prescription of anabolic steroids (tonics, etc) displays our ignorance or irresponsibility; apathy and indifference towards such medically irrational practices.

Different anabolic steroids are promoted in various parts of the third world (including India) for vague indications like overcoming of loss of weight, poor general health, wasting illnesses, to aid malnourished children (drug experts have emphasised that these products can help transform food to body protein **only** if the patient is getting enough food, particularly enough protein and total calories)

- for treatment of debility and emaciation.
- senility, muscular dystrophy
- for eppetite improvement
- for pernicious anaemia, lack of energy
- poor weight gain
- reduced resistance to infection
- tiredness and debility, lack of stamina and listlessness

According to the British National Formulary "the use of anabolic steroids as body builders or tonics is quite unjustified."

According to AMA Drug Evaluations, the use of anabolic hormones to improve athletic performence is unanimously condemned. Besides the fact that there is "no increase in the size and strength and in the muscle size, there is an added risk of liver damages and interference with the testicular function".

What is more objectionable is that the "indications for use" and the "warnings about the drug" very in defferent countries depending on the effectiveness of the country's controlling authorities and the general awareness of the medical community and the public".

The three most popular brands of anabolic steroids are :

- Winstrol = a form of stanozol by Winthrop, USA
- Durabolin = a form of nandrolone phenpropoinate by Organon
- Dianabol = a form of methandrostenolone by CIBA GEIGY

Some of the other brands avilable in India, the drug houses are :

OROBOLIN DROPS

- By Organon, which promoted Orbolin drops in Bangaldesh "for paediatric use in conditions like marcismus, malnutrition, poor weight gain, retarded growth - kwashiorkoi, etc.

According to Diana Melrose in her working paper "Medicines and the Poor in Bangladesh".

Durabolin and Decadurobolin "stimulate the appetite, ensures adequote food intake....checks protein depletion....resistance against infectious diseases and improves general constitution and restores a sense of well being". They also cause "no fluid retention and free from harmful effects on the liver".

In the UK doctors are told "not recommended for children". Warnings include "anabolic steroids may cause fluid retention". Tumours of the liver have been reported occasionally.

Relative costs are given in the Appendix. Numerous tonics contain anabolic steroids - an exhaustive list needs to beprepared. The Pune Journal of Continuing Medical Education of June 1982 gives and editorial on CIBA GEIGY withdrawing Dianobol. We can make sure this is really done and that others follow suit.

ANABOLIC STEROIDS FOR GROWTH

Brand & Drug House	Ingredients	Cost	Indications	Dosage	Contraindications & Spl. Precautions
* Adroyd (Parke-Davis)	Oxymetholone 5mg	15-9.04	Underweight or asthenic patients convalescence from acute infectious disease, major surgical procedures - pre - and post-operatively, chronic debilitating illness; osteoprorosis, fractures and decubitus ulcers, severe burns	Occassionally 20-30 mg. daily may be required. Usually for 10-21 days but not more than 90 days. Ped. dosage: see Lit.	Prostatic carcinoma. Although lAdroyd has a ow degree of androgenicity, very young and preadolescent individuals are usually sensitive to the masculinising effects of androgens. Due to this, they should be under medical supervision during therapy and the drug withdrawn if masculinising effect develop. Adroyd should be used with caution in cardiac disease, hepatic dysfunction, nephritis and nephrosis.
* Anabolex B 12 (Cipla)	Methandienone 2mg Vit B12 50mcg ferric amm. cit. 50mg/ml	5ml-6.23	Loss of appetite and weight loss with anaemia. Growth disorders in children	15-10 drops daily for 4-6 weeks	Continuous treatment should be limited to a max. of 4 weeks with intervals of 1-2 months between courses.
* ‖ Dianobol (Ciba-Geigy)	Methandienone 25 mg	1ml-5.70	Hegative nitrogen-balance, protein malnutrition, convalescence, wasting diseases, osteoporosis, growth retardation, aplastic anaemia, red-cell aplasia.	1ml-i.m. weekly. For intensive therapy 1ml on alternate days	Prostatic cancer, severe liver insufficiency, severe nephrosis, pregnancy and lactation. Should not be given continuously for persons periods exceeding 4 weeks. High doses in women may produce menstrual cycle disorders, hirutism, deepening of voice. In children, premature ossification of epiphyses and virilisation may occuir.

BRAND & DRUG HOUSE	INGREDIENTS	COST	INDICATIONS	DOSAGE	CONTRAINDICATION & SPL. PRECAUTIONS
*☐ Dianabol Tabs (Ciba-Geigy)	Methandienone 1 mg and 5 mg	1mg : 20-%.53 5mg : 10-6.02	(Same as Dianabol)	Male : 5mg daily. Maint. therapy: 2.5 mg daily. See Lit Female: 2.5mg daily. Maint: 1-2mg daily. See Lit.	(Same as Dianabol)
*☐Dianabol Drops (Ciba-Geigy)	Methandienone 1 mg per ml	5ml-5.50	(,,)	Children: 0.01 - 0.04 mg/kg body wt for not more than 4 weeks	(,,)
☐ Durabolin (Organon)	Nandrolone phenyl propionate ; 10 mg and 25 mg	10mg-13. 25mg-21.85	Protien loss following surgery trauma, burns, infectious diseases or following prolonged corticosteroid therapy, uraemia due to acute and chronic renal failure, general debility, osteoporosis, aplastic anaemia, inoperable mammary careinoma, under weight children and fractures.	1.m. 25 mg every week In acute renal failure upto 50mg and daily in chronic renal insufficiency upto 50 mg twice weekly. Children: 10mg every week	(See lit)
☐ Deca Durabolin	Nandrolone decanoate 10 mg and 25 mg	10mg : 1 amp -9.28 25mg: 1 amp 8.53	1.m. 25mg every 3 weeks. In acute renal failure upto 50mg weekly and in chronic renal insufficiency upto 10mg every 3 weeks. Children : 10mg, every 3 weeks		

* MIMS *N.B.* Dianabol has been deleted from the June issue of MIMS and is withdrawn by Ciba-Geigy.
☐ CIMS

BRAND & DRUG HOUSE	INGREDIENTS	COST	INDICATIONS	DOSAGE	CONTRAINDICATIONS & SPL. PRECAUTIONS
*□ Evabolin (Concept)	Nandrolone phenyl-propionate 25 mg Vit. E 100 mg/2ml	2ml-7.06	Convalescence, to promote growth in undernourished children adjuvant to steriod therapy, Osteoporosis, hypoproteinaemia, Haemolytic anaemias.	2ml-4ml i.m. once weekly	Carcinoma of prostate, pregnancy, male breast carcinoma.
* Neurabol H (Cadila)	Vit B1 60mg B6 27.5 mg Hydroxycobalamin 100 mcg. nandrolone phenylpropionate 25 mg/2ml	2ml-4.42	General debility, osteoporosis, weight loss, refractory anaemias, neuritis, neuralgias.	2ml i.m. every week	Prostatic carcinoma, pregnancy B1 sensitive patients
*□ Orabolin (Organon)	Ethylestrenol 2 mg	20-13.34	Osteoporosis, weight loss debility, anorexia burns, during steroid therapy	1 tab twice daily. In serious conditions dosage may be increased.	Pregnency, Prostatic carcinoma, male breast carcinoma. Severe liver dysfunction.
*□ Orabolin Drops (Organon)	Ethylestrenol 2mg per ml	5ml-6.56	Body wt upto 10 kg	Body-wt upto 10 kg : 10-20 drops. 10-20 kg:20-40 drops 20-30 kg:40-50 drops More than 30 kg : 50-60 drops. All daily	
* Trinergic (Unichem)	Methandienone 5 mg, Vit B1 10mg B6 10 mg B12 30 mcg	20-12.71	Malnutrition and under nutrition convalescence, old age anorexia nervosa, neurological disorders, extensive burns, severe injuries.		Continuous treatment should be limited to a max. of 4 weeks with intervals of 1-2 months between courses.
* Trinergic Inj. (Unichem)	Methandienone 25 mg Vit B12 500 mcg/ml	1ml-2.96	(Same as above)	1ml once or twice weekly.	(Same as above)

* MIMS □ CIMS

Brand & Drug House	Ingredients	Cost	Indications	Dosage	Contraindications & Spl. Precautions
* □ Unabol (Unichem)	Nandralone phenyl propionate 25mg/ml	1ml-7.01	Negative nitrogen balance, oldage, osteoporosis, bone fractures, during prolonged corticosteroid therapy, to promote weight gain	25mg weekly	Carcinoma of prostate, pregnancy, male breast carcinoma
* □ Winstrol (Cosme Farma)	Stanozolol 2mg	20-12.46	Poor protein anabolism, osteoporosis, convalescence, aplastic anaemia, during corticosteroid theraphy.	2-4mg thrice daily just before or with meals. Children 3-6 years : 1mg twice daily; 6-12 yrs: 2mg. thrice daily	Pregnancy, carcinoma of prostate, Severe liver disease. Pre-pubertal children where it may lead to stunting of growth. Use lower dosage in young females to minimise androgenic side-effects. Impaired cardiac and renal function.
*Aquaviron B12 (Nicholos)	Free testosterone 25mg, Vit B12 500mcg per ml	1ml-4.75	Depressed debilitated male patients	1ml i.m. twice weekly for about 6 weeks; diminish frequency as conditions improves	Prostatic carcinoma
* Aquaviron Inj (Nicholos)	Free testosterone 25mg/ml	1ml-2.50	Male : hypogonadism, organic impotence, eunuchism delayed puberty, premature senility. Female : metropathia haemorrhagiea menorrhagiea, frigidity, inoperable breast carcinoma	Male: 1-2ml every 1-2 weeks diminishing the dose as patient improves Female : 1-2ml daily until bleeding stops. Not more than 200mg in one month	

* MIMS □ CIMS

Courtesy : V. H. A. I., New Delhi

WHY AMIDOPYRINES MUST GO

Drugs have come to form the basis (most emphasised part) of medical care today. There is increasing drug dependence, the case with which even potentially dangerous drugs can be obtained freely over the counter - with no warning whatsoever, is well known. It is all this that makes the need for drug information sharing with the health personnel and the consumers the responsibility of individuals and groups concerned with "health" and issues related to health.

The question here is not merely of free availability of hazardous drugs with inadequate information but it is also a question of the fact that many others are deprived of essential and life saving drugs.

Amongst the most widely used drugs are the analgesics and amongst some of the more popular brands are drugs containing analgin. The irrationality of most combination drugs has been adequately shown and a WHO Expert Committee on the selection of essential drugs disapproved of their use.

This paper reviews some of the facts about analgin from medical text books and medical journals. Some of these facts are not divulged by the producers and sellers of these drugs and even if divulged it is done in such an ambiguous manner that either it is not understood or not taken seriously.

Aminophenazone (amidopyrine, aminopyrine) has been used for its potent anti-inflammatory and analgesic action for more than 70 years.

Till 1933 casual relationship between aminophenazone and agranulocytosis had not been established.

(Madison F. W., and Squier, T. L. (1934) : Etiology of Primary Granulocylopaemia Agranulocytic Angina) : JAMA 102 : 755-759

Within 2 years 70 fatal cases were published.

(Plum, P. -1935) Agranulocytosis due to amidopyrine (an experimental and clinical study of 7 new cases) : The Lancet 1, 14-21

Reviews provided evidence to suggest that over 90% of all cases of agranulocytosis reported in medical literature over the previous four years had been associated with aminophenazone.

(Kracke, .R.R. and parker, F.P.-1935): Relationship of Drug Therapy and Agranulocytosis : JAMA 105, 960-966.

According to WHO Drug Information-Jan - March 1977 : PDT/DI/77.1

"Recognition of the danger grertly reduced the use of aminophenazone in several countries **before** the first decision to place it under **prescription control** was announced in 1938 by FDA in the USA.

Amidopyrine (also known as aminophenazone) was considered the major cause of agranulocytosis in the 1930's (Jackson & Tighe 1939.) However, following the ban on its sale by many countries, it is now one of the less common causes,**This is only true for such countries, which have banned the drug· But not so in other countries like India where these drugs are sold like toffees and over the counter under 90 brand names which give no clue to the content

** G.C. deGruchy : ' Drug Induced Blood Dyscrasias" -1975).

Amidopyrine

Aminopyrine,
Aminophenazonium, Amidozofen
Di methyl aminophenazone,
4Di methylamino 1, 5 dimethyl - 30 x 0 - 2

Phenylpyrazoline (Noramidopyrine methanesulphorate --has the same toxicity).

(WATCH OUT for any of the above names as a content in any analgesic you take!!)

> "**The risk of agranulocytosis** in patients **taking amidopyrine is sufficiently great to render this drug unsuitable for use.** Administration of large doses of amidopyrine has been associated with renal tubular necrosis"
>
> — Martindale —

From 960 patients treated with amidopyrine there were 11 cases of agranulocytosis -an incidence of 1.1%. **These figures did not justify** using amidopyrine in **ordinary practice as an analgesic.** Most cases of Amidopyrine agranulocytosis arose from the use of proprietary medicines containing the drug, where the prescriber was ignorant of, or forgot, its presence.

Association of Clinical Pathologists : The Lancet 1/1951 : 389

Amidopyrine might cause toxic epidermal necrosis : R. L. Baer and H. Harris
JAMA - 1967, 202, 710

> "**Amidopyrine and nor-omidopyrine induced agranulocytosis has high mortality and neither drug is essential.** The only possible indication are febrile convulsions in children and rare cases of uncontrollable pyrexia in malignant disease."

The grave hazard of theraphy with amido-pyrine and noramidopyrine could be greatly reduced by proper control of the sale of these dangerous drugs. Fatal agranulocytosis has even occurred in the new born as a result of consumption of amidopyrine by the mother before delivery.

The clinical presentation is usually fulminating with severe oro pharyngial ulceration fever prostration and circulatory failure. Death may occur from overwhelming sepsis despite treatement with corticosteroids, antibiotics and blood transfusions.

Side Effects of Drugs

Royler & Herxheimer 1968-1971.

Other side effects given are :

- — Allergic reactions to skin
- — Anaemia
- — Anorectal ulceration and necrosis (with amidopyrine suppository)
- — Chronic gastritis
- — Fatal renal failure
- — liver damage
- — Drowsiness, coma, convulsions and decerebrate rigidity have been described in cases of intoxication involving amidopyrine.

> "Amidopyrine is justified only in serious or life threatening situations where no alternative antipyretic is available or suitable".
>
> — Martindale p. 191

The WHO Expert Committee considers analgin and other analgesics or combinations as effective (if not less) as aspirin (which is sbout 9-10 times cheaper). The WHO Committee which formulated the list of essential drugs excluded amidopyrines on grounds of their toxicity.

Pyrazolone derivatives

Antipyrine (Phenazone)
Isopropylantipyrine
Dichlorophenazone

WHO PDT/D1/77.1

These contain the same "phenazone" neucleus which is important in pathogenesis of agranulocytosis and though agranulocytosis is much less with antipyrine they cannot be assumed to be safe.

In the 1960's close relatives of amidopyrine, pyrazalone, noramidopyrine (dipyrene, metamazole) became very popular.

At present, the above are only approved for use in serious conditions in which other drugs were ineffective and on the understanding that all preparations would carry the warning label. This drug may cause fatal agranulocytosis. Though no formal restriction has been imposed on the sale of aminophenazone, it is no longer available in the USA, since none of the compounds containing it are registered.

Further fatal cases of agranulocytosis have led to the withdrawal of the substance according to WHO PDT/D1/77.1.

The incidence and risk of potentially fatal agranulocytosis far outweigh any benefit that can be derived from its use.

Drugs for Human use containing Dipyrone Federal Register (1976) 41, No. 173 37386 - 37388

There is no justification for using oral or parentral dipyrone or aminopyrine for reduction of fever unless aspirin and other safer anti pyretics are ineffective, poorly tolerated, or cannot be taken orally.

Due to interaction of aminophenazone and nitrites in the stomach a carcinogenic substance dimethylentrosamine may lead to malignant tumours in the liver and the lung. This potential hazard has been the reason of banning the drug in some countries.

The severe and lethal blood damage with aminopyrine is well known by physicians in the west. There, another agent called dipyrone under such names as metamizol, noramidopyrine sulpyrine and metampyrone was pushed. In the 1973 edition of the AMA Drug Evaluations, American physicians were advised that :

"There is evidence that dipyrone, a derivative of aminopyrine that shares its potential for toxicity, unfortunately is still being misused. This is probably because it is available in injectable form and because physicians do not recognize its similarity to aminopyrine since it is marketed under various trade marks. Its only justifiable use is as a last resort to reduce fever where safer measures have failed. Because dipyrone may produce fatal agranulocytosis, and other blood dyscrasias, its use as a general analgesic, antiarthritic or routine antipyretic cannot be condoned".

(page 262 - 267)

In 1977 it was stated that the drug had become obsolete in the USA (page 341). In the 1980 edition it is **not even listed.**

Prescriptions for Death Drugging of the Thirld World (Milton Silverman ; Philip R. Lee ; Mia Lydecker) University of California Press.

An international Study of Drug-induced Agranulocytosis and Aplastic Anaemia, funded by Hoechst, is being undertaken, inter alia, in Israel, Germany, Italy and Brazil. The results are expected in April 1983.

In the opinion of Dr. A. Herxheimer of Charing Cross Hospital Medical School, UK, and Prof. John Yudkin : "The study seems very well designed to detect any associations between drug history and the development of agranulocytosis. However, we fear that Hoechst may claim that the results can provide a figure for the true incidence of drug-induced agranulocytosis. In fact, of course, the study will excluded all patients

(1) who die of agranulocytosis without receiving medical care.

(2 who die of it without having had a white-cell count.

(3) who have undiagnosed agranulocytosis and recover from it."

Dr. Herxeimer and Prof. Yudkin feared that the proportion of cases so excluded in each category would be higher in countries with poorly developed medical care. Consequently, they felt that the study would yield only a "**minimum estimate**" of both "incidence and mortality", while the „actual incidence coudl

be considerably higher". They therefore wis hed to "impress Hoechst with this point,so that they are not tempted to talk about "incidence of agranulocytosis" when describing the results of the study".

Dr. Herxheimer explained these fears to Sir Richard Doll, one of three 'unpaid advisory committee' members to monitor, on behalf of Hoechst, the results of the abovementioned study. Sir Richard opined that "the purpose of the setting up of our committee was just to ensure that the scientific report took account of the sort of points you mention What Hoechst does with the report, of course, is another matter over which none of us can have any control". This left the multinational a free hand to do what it liked!

The dangers inherent in the use of amidopyrine ann noramidopyrine were later (March 1981) expressed by Dr. Herxheimer in a letter to Dr. A. R. Scott in Tanzania. Dr. Herxheimer said: "Amidopyrine carries an unacceptable risk of agranulocytosis, and many people believe that this is true also for noramidopyrine (Novalgin). He added, however, that "Hoechst hope to argue that the incidence of deaths from marrow damage will be much less than that from bleeding with aspirin or from self-poisoning with paracetamol, and that the drug is therefore a wonderful alternative. I find that argument hard to accept, and prefer to do entirely without noramidopyrine, at least for the present".

WHO recognized that the risk of agranulocytosis arising from the use of pyrazolone derivatives is assessed very differently from country to country even within Europe. In the case of aminophenazone, the incidence in the UK (based on data in 1952) was 0.8%, whereas data from the Federal Republic of Germany in the mid-1960's placed the comparable risk at 1 : 10,000. Although the frequency of the reaction was calculated at 1 : 100,000 50% of the cases ended fatally and children were shown to be as vulnerable as adults.

(WHO DRUG INFORMATION - PDT/ DI/77.1 : Jan-Mar 1977 : p. 10)

According to preliminary investigations in some countries of Europe and Latin America, 124 cases of agranulocytosis and 82 cases of aplastic anaemia were notified between July 1, 1980 and June 30, 1981.

ACTION IN OTHER COUNTRIERS AGAINST

DIPYRONE : Generic Names - Metamizol Metampyrone, Noramidopyrine, Methanesulphonate Sodium and Sulpyrine. Some brand names are-Cormel (Winthrop) and Novalgin (Hoechst)

These are **BANNED** from **Sale** in Australia, Sweden, UK. They are **not available** in the USA since it is not listed in the PDR. They are left for very limited indications and taken off all common cold medicines, antipyretic-analgesics, etc. in Japan, the Philippines and Denmark. All preparations for intravenous and intramuscular injections containing more than 1 gm per vial have been withdrawn in Italy.

Bangladesh has **banned the manufacture and sale of amidopyrines** along with 1707 other hazardous drugs.

In India, in 1979, the Drug Controller, asked manufacturers to gradually withdraw amidopyrine. No deadline was set. Consequently, it continued to be produced and marketed without even adequate warning about its side effects. By August 1980, 33 formulations containing amidopyrine, were being marketed. When the Maharashtra FDA banned amidopyrine, the multinational company producing it got a stay order from the court arguing that it was being manufactured and marketed in other states.

Writing in the Lancet on 14th November 1981, Prof. John Yudkin said that between July and November 1980 it proved possible to obtain CIBA - GEIGY manufactured drugs containing amidopyrine in 11 countries, including. This was despite CIBA GEIGY's announcement

in SCRIP of August 11, 1980 that their decision to replace amidopyrine with propyphenazone in all their products" has been taking place worldwide at a pace compatible with the complexities of the risk". Moreover, Prof. Yudkin added, there was evidence that CIBA - GEIGY continued to manufacture preparations containing amidopyrine and that old stocks were being sold off even after registering the new formulations. He cited the example of having purchased cibalgin containing amidopyrine in February 1980 — two years after the date given for reformulation.

And, it is well known that cibaig n is still available in India over the counter-just for the asking !

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DRUGS CONTAINING ANALGIN

	BRAND	DRUG HOUSE
*☐	Anadex	Concept
*☐	Baralgan	Hoechst
*☐	Benalgis	Franco-Indian
*	Combigesic	Unloids
☐	Cemizol Inj	IDPL
*☐	Cibolgin Compositum	Ciba-Geigy
☐	Conaril	Citadel
☐	Dolagin +	Pharmed Gujarat
*	Eucrasil	Eisen
*	Eucrasil — 5	Eisen
*	Eucrasil Forte	Eisen
☐	Fargesic	PharEast
☐	Fargesic Syrup	PharEast
☐	Maxigesic	Ethico
☐	Medalgin	Medoz
☐	Medalgin Syrup	Medoz
☐	Neogene	Anglo-French
☐	Novalgin	Hoechst
☐	Novalgin Injection	Hoechst
*	Promalgin	Uniloids
*☐	Sedyn-A-Forte	M M Labs
*	Spasmizol	IDPL
*	Spasmizol Drops	IDPL
*	Spasmizol Inj.	IDPL
*☐	Ultragin	Manners
*☐	Ultragin Syrup	IDPL
*☐	Ultragin Inj.	IDPL
*☐	Zimalgin	Rallis

DRUGS CONTAINING PHENACETIN

*	Capherin	Mercury
☐	Dolopar	Micro
*☐	Dolviran	Bayer
*☐	Treupel	German Remedies
*☐	Veganin	Warner

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* MIMS APRIL 1982

☐ CIMS MAY 1982

Courtesy : **V.H.A.I.**
New Delhi

in SCRIP of August 11, 1980 that their decision to replace amidopyrine with propyphenazone in all their products" has been taking place worldwide at a pace compatible with the complexities of the risk". Moreover, Prof. Yudkin added, there was evidence that CIBA - GEIGY continued to manufacture preparations containing amidopyrine and that old stocks were being sold off even after registering the new formulations. He cited the example of having purchased cibalgin containing amidopyrine in February 1980 — two years after the date given for reformulation.

And, it is well known that cibaig n is still available in India over the counter-just for the asking !

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DRUGS CONTAINING ANALGIN

	BRAND	DRUG HOUSE
*☐	Anadex	Concept
*☐	Baralgan	Hoechst
*☐	Benalgis	Franco-Indian
*	Combigesic	Unloids
☐	Cemizol Inj	IDPL
*☐	Cibolgin Compositum	Ciba-Geigy
☐	Conaril	Citadel
☐	Dolagin +	Pharmed Gujarat
*	Eucrasil	Eisen
*	Eucrasil — 5	Eisen
*	Eucrasil Forte	Eisen
☐	Fargesic	PharEast
☐	Fargesic Syrup	PharEast
☐	Maxigesic	Ethico
☐	Medalgin	Medoz
☐	Medalgin Syrup	Medoz
☐	Neogene	Anglo-French
☐	Novalgin	Hoechst
☐	Novalgin Injection	Hoechst
*	Promalgin	Uniloids
*☐	Sedyn-A-Forte	M M Labs
*	Spasmizol	IDPL
*	Spasmizol Drops	IDPL
*	Spasmizol Inj.	IDPL
*☐	Ultragin	Manners
*☐	Ultragin Syrup	IDPL
*☐	Ultragin Inj.	IDPL
*☐	Zimalgin	Rallis

DRUGS CONTAINING PHENACETIN

*	Capherin	Mercury
☐	Dolopar	Micro
*☐	Dolviran	Bayer
*☐	Treupel	German Remedies
*☐	Veganin	Warner

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* MIMS APRIL 1982

☐ CIMS MAY 1982

Courtesy : **V.H.A.I.**
New Delhi

USING TETRACYCLINE FOR CHILDREN & PREGNANT WOMEN

INTRODUCTION

The question of Syp. tetracycline for paediatric usage is not merely one of discolouration of the teeth. More importantly, it is the question of **Selling and prescribing a potentially Harmful drug without giving adequate information to the patient.** It is also a question of the over use or misuse of a drug in trivial conditions when, more often than not, it is not required; and of attempting to deal with childhood infection with pills, while the causes of the infection and increased susceptibility are allowed to remain untouched.

Looking at the drugs we prescribe or consume makes us realise the necessity to know more about these drugs–not from the drug representative but from authentic medical literature and the experience of others. Realization of this discrepancy in the information from the drug companies and their medical literature enhances our responsibility in this regard to the patients.

Rational therapeutics is knowledgeable prescribing of the most effective, least costly, most non–toxic, easily available drug in the right quantity, for the right duration and for the right problem in the right way.

It is the responsibility of health personnel to ensure that the right drugs are produced and made available to those who most need them, and that hazardous or irrational drugs are thrown out of the market.

Ensuring that people get at least the minimum required to be healthy is our MAIN CONCERN. We realize that drugs can play only a small part in keeping people healthy. Therefore, by demolishing some of the myths surrounding the unquestionable healing properties of all drugs, we hope more and more individuals will begin to look beyond pills for a cure for their ills.

The manufacture of Tetracycline for paediatrics is supposed to be banned from January 1982. The date of the ban on marketing of the drug has not yet been fixed. The reasons for banning the manufacture are :

1. DENTAL DISCOLOURATION

"Children receiving long or short term therapy with tetracycline may develop brown discolouration of the teeth. The larger the dose of the drug relative to body weight, the more severe is *the deformity, the deeper the colour, and the more intense the hypoplasia of enamel"* The quantity received is more important than the duration. *Mild darkening of the* permanent teeth occurred in *3 of 14 children* who received 5 courses of the drug, whereas 4 of 6 who received eight courses had *moderate darkening* of the enamel.

> (Ref : Grossman, E.R., Walchick, A; Freedman, H. : Tetracycline and Permanent Teeth : the Relationships between doses and tooth colour : Paediatrics : 1971, 47, 567–570).

"The risk of this is highest when the tetracycline is given to neonates and babies prior to the first dentition".

"If given between the ages of 2 *months and 5 years-pigmentation of the permanent teeth* may develop."

The earliest characteristics of this defect is yellow fluorescence probably due to the formation of a tetracycline–calcium orthophosphate complex; with time this progresses to permanent brown pigment.

2. CATABOLIC EFFECT

"Tetracyclines exert a catabolic effect, perhaps due to a generalized inhibition of protein synthesis in mammalian cells".

"Administration of 2.5 to 3 gms. of Chlortetracyclines given to under nourished adults results in weight loss, incre-

ased urinary nitrogen excretion, negative nitrogen balance, and elevated servum non protein nitrogen concentration."

(Goodman Gillman : page 1188 6th Ed)

Gocke, T.M., Jackson, G.G , Grigsby, M.E., Love, B D. Jr, and Finland, M.

"Some effects of antibiotics on nutrition in man, including studies of the bacterial flora of the faeces". Arch. Intern Med. 1958, 101, 476-513.

In India the majority of children who would receive tetracycline are malnourished or bordering on malnutrition. They would be repeatedly picking up infection more often viral but bacterial infections as well. Additionally, how much of this drug would get prescribed by different doctors or consumed anyway, we don't know.

3. BONE GROWTH

According to Goodman, Gillman, 6th Edition (1980) Tetracycline are deposited in the skeleton of the human foetus and young child. A 40% depression of bone growth, as determined by the measurements of fibula, has been demonstrated in premature infants treated with these agents. (Cohlan, S Q., Bevelander, G , and Tiamsic, T. : Growth Inhibition of Prematures Receiving Tetracyclines-Clinical and Lab. investigations.
Am. J. Dis. Child 1963, 105, 453–461).

4. Tetracycline induced diarrhoea is not exactly uncommon and that supra-infection by other organisms may occur some times.

5. "Tetracycline may cause increased intracranial pressure and tense bulging of the fontanels (pseudo tumor cerebri) in young infants, even when given in usual therapeutic doses".

(Ref : Goodman, Gillman)

Increased intracranial pressure presents itself with severe headache, vomiting, loss of function of certain cranial nerves, and limbs and if severe, even death. The figures of how common or rare this entity is, are not available to us right now.

6. The ingestion of out dated and degraded tetracycline is known to cause Fanconi Syndrome – a clinical picture characterized by nausea, vomiting, polyuna (increased passage of urine, polydipsea–increased thirst, acidosis, protienuria glycosuria and aminoacidune (passage of proteins, glucose and aminoacids in urine).

Our drug control of sales of hazardous drugs, sales of out–dated products is not exactly good and whether the problems created by out–dated tetracycline is more than discolouration of the teeth would be interesting to know.

PREGNANT WOMEN

Liver Damage :

According to Goodman, Gillman: "Pregnant women appear to be particularly susceptible to severe, tetracycline–induced hepatic damage".

Schultz, J.G , Adamson, J.S., Jr: Workman, W.W., and Morman, T.D. Fatal Liver Disease after intra-venous Administration of Tetracycline in high Dosage N. Eng J. Med 1963: 269, 999–1004.

"Jaundice appears first, and azotemia acidosis and irreversible shock may follow. Although hepatic fat is increased during pregnancy, the quantity appears to be even greater after exposure to a tetracycline.

"Disseminated intravascular coagulation has been reported in a pregnant woman who developed hepatic renal failure after given only 2 doses of 100mg. each of tetracycline intramuscularly (Pride, G L , Cleary R. E. & Hamburger, R J. Disseminated intravascular coagulation associated with tetracycline induced hepato renal failure during pregnancy. Am J. Obst. Gynae. 1973, 115, 585-586). This may be a rare phenomenon.

"Treatment of pregnant patients with tetracyclines may produce *discolouration of teeth in the offspring*. Ingestion of the drug between mid-pregnancy to about *4-6 months of post natal period* is dangerous for deciduous anterior teeth (temporary front teeth) and from 6 months to

5 years of age for the permanent anterior teeth. Children up to 7 years may be susceptible to this complication of tetracycline therapy".

(Weyman, J. Tetracycline and Teeth. Practitioner 1965, 195, 661-665)

The argument offered for continuing its use is that Tetracycline is cheap, easily available.

In Australia, the Drug Evaluation Committee has recommended the banning of all tetracyclines in paediatric formulas.

In Belgium, the Philippines, Italy and the U.S.A. the drug has been banned from Paediatric formulas. In addition, there is the compulsory warnings: Not to administer in pregnancy and to children below 8 years.

The International Organization of Consumer Unions has listed Tetracycline as one of the 44 problem drugs, rated as a widespread serious problem.

Tetracycline is a more expensive drug than penicillin or sulphonamides, It is a bacteriostatic drug. For many infections it is not so good. The yellowness of the teeth can be seen only months or years later, and it lasts all through the patient's life.

A mother should not be given tetracycline after four months of pregnancy, nor should a child be given the drug if he is below 7 years, unless his life is in danger

The Editorial board of JCMAI has resolved to bring out a new feature on *Institutional News* subject to the following conditions.

Hospitals to be asked to contribute Rs. 100 for this service which will include the following :

(a) Occupy one page of the Journal

(b) One photograph may be included

(c) Limited number of re-prints may be provided free of cost. Further re-prints will be made available at extra cost, upto two institutions may be so publshed in any issue of the Journal.

BRANDS CONTAINING TETRACYCLINE

ANTIBIOTICS

Brand & Drug House	Ingredients	Cost	Dosage	Contraindications & Spl. Precautions
Ificyclin Paed. drops (Unique).	Tetracycline 100mg./ml.	5ml– 1.81 10ml– 3.35		In childhood it can cause permanent discolouration of the child's teeth & therefore prolonged use should be avoided.
Ificyclin Syrup (Unique)	Tetracycline 100mg. per 5ml.	25ml– 2.44 50ml– 4.39 450ml–32.24		
Linemett Syrup (Mercury)	Tetracycline 125mg. per 5ml.	30ml– 3.18 60ml– 5.87	333mg-1g 8-12 hourly Children : 20mg/kg body-wt in divided doses daily.	Renal failure. Prescribed with caution to children under 6 years. ++ (See Sec. 7 A)
*Lupicyclin Syrup (Lupin)	Tetracycline 125 mg.	30ml– 4.60 60ml– 8.13 500ml–41.17	250mg 6 hourly. Children : 20-40mg/kg body wt in divided doses.	++ (See Sec. 7A)
*Mysteclin-V Paed. Drops (Sarabhai)	Tetracycline hcl 100 mg. amphotericin B 20 mg./ml.	10ml– 2.91		++ (See Sec. 7A)
*Sandocycline Susp. (Sandoz)	Tetracycline 125 mg. broxyquinoline 200 mg. brobenzoxaldine 40 mg / 5 ml.	60ml– 6.05	2.5-10ml 6 hourly according to age. See Lit.	Renal disease. Concurrent admin. of other hepatotoxic drugs. ++(See Sec. 7A)
* ⊩ Subamycin Paed. Syrup (Dey's)	Tetracyline 125 mg./5ml.	40ml– 4.91	12.5-25mg/kg body-wt daily in 4 divided doses	++(See Sec. 7A)
* ⊩Subamycin Drops (Dey's)	Tetracycline 100mg /ml.	5ml– 2.71 10ml– 3.47		"

Brand & Drug House	Ingredients	Cost	Dosage	Contraindications & Spl. Precautions
* ǂ Terramycin Soluble Tabs (Pfizer)	Oxytetracycline hcl 50mg.	25ml– 3.15	Children: 20mg/kg body wt in equally divided doses every 6 hourly	++ (See Sec. 7A)
* ǂ Terramycin Syrup (Pfizer)	Oxytetracycline 125mg/5ml	30ml– 3.70 60ml– 6.32	20–55mg/kg body wt daily in 4 divided doses.	"
* ǂ Terramycin Paed. Drop (Pfizer)	Oxytetracycline 100mg/ml	5ml– 2.58 10ml– 3.59		"
* ǂ Terramycin I M Inj. (Pfizer)	Oxytetracycline 50mg/ 125mg/ml	50mg:2ml– 1.06 10ml– 3.59 125mg:2ml– 1.57	200–400mg daily in divided doses every 6–12 hrs. Children: 7–10mg/kg body wt daily.	"
* Terramycin I V Inj. (Pfizer)	Oxytetracycline	3ml– 2.90	250–500mg 12 hourly. Maximum 250 mg 6 hrly. Children: 10–20mg/kg body wt daily in 2 divided doses. Maximum 30mg/kg body wt daily in 3–4 divided doses.	"
* Trycin (MSD)	Tetracycline hcl 250 mg	4ml– 2.20	250mg 6 hrly. Children: 26–60mg/kg body wt. daily in 4 divided doses	"
ǂ Alcyclin Paed, S Drops (Alembic)	Tetracycline hcl 100mg/ml (approx 20 drops)	5ml– 2.27 10ml– 3.05	10–30mg per kg body wt, daily in 4 equally divided doses according to severity of infection.	Prolonged & frequent use in children
ǂ Alcyclin-O (Alembic)	Oxytetracycline equiv to anhydrous oxytetracycline 50mg. lidocaine 2% per ml vial & 250 mg per 2ml with lidocaine 2%	250mg: 10 x 2ml–13.94	Children and infants : 10–15mg per kg body wt per day in 2–3 equal divided doses i.m. 250mg: lamp deep i.m. every 9–12 hrs.	

* MIMS ǂ CIMS

++ SEC 7A : Tetracycline should not be used in the latter half of pregnancy. or in children upto 12 years of age. Use with extreme caution in impaired renal or hepatic function; dosage should be reduced accordingly. The simultaneous administration of milk supplements containing salts of calcium, magnesium or iron should be avoided.

MODEL LIST OF ESSENTIAL DRUGS
Explanatory Notes

I. The numbers preceding the drug groups and sub groups in the model list (e.g., 11; 17.6.2) have been allocated, in accordance with the English alphabetical order, for convenience in referring to the various categories; they have no formal significance.

II. Numbers in parentheses following the drug names indicate :

(1) Listed as an example of this therapeutic category: choose cheapest effective drug product acceptable;

(2) Specific expertise, diagnostic precision or special equipment required for proper use;

(3) Greater potency;

(4) In renal insufficiency, contraindicated or dosage edjustments necessary;

(5) To improve compliance;

(6) Special pharmacokinetic properties for purpose;

(7) Adverse effects diminish benefit/risk ratio;

(8) Limited indications or narrow spectrum of activity;

(9) For epidural anaesthesia;

(10) Drugs subject to international control under the Single Convention on Narcotic Drugs (1961) and the Convention on Psychotropic Substances (1971).

III. Letters in parentheses following the drug names indicate the reasons of *complementary drugs :*

(A) When drugs in the main list cannot be made available;

(B) When drugs in the main list are known to be ineffective or inappropriate for a given individual;

(C) For use in rare disorders or in exceptional circumstances.

IV. When the strength is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as".

V. All drugs listed in this formulary are itemized by their *generic* names as an aid to encourage the use of generic names in prescribing and ordering medicines.

Main list	*Complementary drugs*	*Route of administration, pharmaceutical forms and strengths*
1. ANAESTHETICS		
1.1. General Anaesthetics and Oxygen		
ether, anaesthetic (2)		inhalation
halothane (2)		inhalation
nitrous oxide (2)		inhalation
oxygen		inhalation (medicinal gas)
thiopental (2)		powder for injection, 0.5 g, 1.0g (sodium salt) in ampoule
1.2 Local Anaesthetics		
bupivacaine (1, 2, 9)		injection, 0.25%, 0.5% (hydrochloride) in vial
lidocaine (1)		injection, 1%, 2% (hydrochloride) in vial
		injection, 1%, 2% + epinephrine 1100 000 in vial topical form 2-4% (hydrochloride)

Main List	*Complementary drugs*	*Route of administration pharmaceutical forms and strengths*

2. ANALGESICS, ANTIPYRETICS, NONSTEROIDAL ANTINFLAMMATORY DRUGS AND DRUGS USED TO TREAT GOUT

acetylsalicylic acid		tablet, 100-500 mg. suppository, 50–150 mg.
allopurinol (4)		tablet, 100 mg.
ibuprefon (1)		tablet, 200 mg.
indometacin		capsule or tablet, 25 mg.
paracetamol		tablet, 100–500 mg. suppository, 100 mg.
	colchicine (B,C) (7)	tablet: 0.5 mg,
	probenecid (B,C)	tablet, 500 mg.

3. ANALGESICS, NARCOTICS AND NARCOTIC ANTAGONISTS

morphine (10)		injection. 10mg(sulfate or hydrochloride) in 1-ml ampoule
naloxone		injection, 0.4 mg (hydrochloride) 1-ml ampoule
	pethidine (A) (1,4,10)	injection, 50 mg (hydrochloride) in 1-ml ampoule

4. ANTIALLERGICS

Antihistaminies

chlorphenamine (1)	tablet, 4 mg (maleate)

5. ANTIDOTES

5.1 General

charcoal, activated	powder
ipecacuanha	syrup, containing 0.14% ipecacuanha alkaloids calculated as emetine

5.2 Specific

atropine		injection, 1 mg (sulfate) in 1–ml ampoule
deferoxamine		injection 500mg (mesilate) in vial
dimercaprol (2)		injection in oil, 50mg/ml in 2-ml ampoule
sodium calcium edetate (2)		injection, 200mg/ml in 5–ml ampoule
sodium nitrite		injection, 30mg ml in 10-ml ampoule
sodium thiosulfate		injection, 250mg ml in 50–ml ampoule
	methylthioninium chloride (c) (Synonym: methylene blue)	injection. 10mg ml in 10-ml ampoule
	penicillamine (c) (2)	capsule or tablet, 250mg

Main list	*Complementary drugs*	*Route of administration, pharmaceutical forms and strengths*
6. ANTIEPILEPTICS		
diazepam		injection, 5mg/ml in 2–ml ampoule
ethosuximide		capsule or tablet, 250mg
phenobarbital (10)		tablet, 50mg, 100mg
		syrup, 15mg/5ml
phenytoin		capsule or tab , 25mg, 100mg(sodium salt)
		injection, 50mg (sod. salt)/ml in 5-ml vial
	carbamazepine (B.C)	tablet, 200mg
	valproic acid (B.C)(2,4,7)	tablet, 200mg (sodium salt)
7. ANTIINFECTIVE DRUGS		
7-1 Amoebicides		
metronidazole		tablet. 200–500mg
	diloxanide(A)	tablet, 500mg (furoate)
	emetine (A.B) (1,7)	injection, 60mg(hydrochloride)in 1ml ampoule
	paromomycin (B)	capsule, 250mg (as sulfate)
		syrup, 125mg (as sulfate) /5ml
7.2 Anthelmintic Drugs		
mebendazole		tablet, 100mg
niclosamide		tablet, 500mg
piperazine		tablet, 500mg (citrate or adipate)
		elixir or syrup (as citrate) equivalent to 500mg hydrate/5ml
tiabendazole		chewable tablet, 500mg
	bephenium hydroxynaphthoate (B) (8)	granules, 5g (equivalent to 2.5g bephenium)
7.3 Antibacterial Drugs		
ampicillin (1,4)		capsule or tablet, 250mg, 500mg(anhydrous powder for oral suspension, 125mg (anhydrous)/5ml powder for injection, 500 mg (as sodium salt) in vial
benzathine benzylpenicillin (5)		injection, 1.44g benzylpenicillin (=2.4 million IU)/5ml in vial
benzylpenicillin		powder for injection, 0.6g(=1 million IU), 3:0g (=5 million IU) (as sodium or potassium salt) in vial
chloramphenicol (7)		capsule, 250mg powder for injection, 1g (as sodium succinate) in vial
cloxacillin (1)		capsule, 500mg (as sodium salt) powder for injection, 500mg(as sodium salt)in vial

Main list	*Complementary drugs*	*Route of administration, pharmaceutical forms and strength*
erythromycin		capsule or tablet, 250mg (as stearate or ethylsuccinate) oral suspension, 125mg (as stearate or ethylsuccinate)/5ml powder for injection, 500mg (as lactobionate) in vial
gentamicin (4)		injection, 10mg, 40mg (as sulfate)/ml in 2-ml vial
metonidazole		tablet, 200-500mg
phenoxymethylpenicillin		tablet, 250mg (as potassium salt) powder for oral suspension, 250mg (as potassium salt)/5ml
salazosulfapyridine (2)		tablet, 500mg
sulfadimidine (1.4)		tablet, 500mg oral suspension, 500mg/5ml injection, 1g (sodium salt) in 3-ml ampoule
sulfamethoxazole + trimethoprim (4)		tablet, 100mg+20mg, 400mg+80mg
tetracycline (1,4)		capsule or tablet, 250mg (hydrochloride)
	amikacin (B, C) (1,4)	injection, 250mg (sulfate)/ml in 2-ml ampoule
	doxycycline (B) (5,6)	capsule or tablet, 100mg (as hydrochloride)- injection, 100mg (as hydrochloride)
	nitrofurantoin (A, B) (4,7)	tablet, 100mg
	procaine benzylpenicillin (A) (7)	powder for injection, 1g (= 1 million IU) 3g (= 3 million IU)

7.4 Antifilarial Drugs

diethylcarbamazine		tablet, 50mg (citrate)
suramin sodium		injection, 1g in vial

7.5 Antileprosy Drugs

dapsone		tablet, 100mg
	clofazimine (B)	capsule, 100mg
	rifampicin (B)	capsule or tablet, 150mg, 300mg

7.6 Antimalarials

chloroquine (1)		tablet, 150mg (as phosphate or sulphate) syrup, 50mg (as phosphate or sulfate)/5ml
primaquine		tablet, 7.5mg, 15mg (as phosphate)
pyrimethamine		tablet, 25mg
quinine		tablet, 300mg (as bisulfate or sulfate) injection, 300mg (as dihydrochloride)/ml in 2-ml ampoule or 250mg (as formiate) in 1-ml ampoule
	sulfadoxine + pyrimethamine (B)	tablet, 500mg+25mg

Main list	*Complementary drugs*	*Route of administration, pharmaceutical forms and strengths*

7.7 Antischistosomals

metrifonate		tablet, 100mg
niridazole (7,8)		tablet, 100mg, 500mg
oxamniquine		capsule, 250mg syrup, 250mg/5ml
	antimony sodium tartrate (B)	injection, 60mg in 1–ml ampoule
	sodium stibocaptate(B)	injection, 500mg

7.8 Antitrypanosomals

melarsoprol (5)		injection, 3.6% solution
nifurtimox		tablet, 30mg, 120mg, 250mg
pentamidine (5)		powder for injection, 200mg (isetionate or mesilate)
suramin sodium		powder for injection, 1g in vial

7.9 Antituberculosis Drugs

ethambutol		tablet, 100-500mg (hydrochloride)
isoniazid		tablet, 100mg–300mg
rifampicin		capsule or tablet, 150mg, 300mg
streptomycin (4)		injection, 1g (as sulfate)

7.10 Leishmaniacides

pentamidine (5)		powder for injection, 200mg (isetionate or mesilate)
sodium stibogluconate		injection, 33%, equivalent to 10% antimony, in 30–ml vial

7.11 Systemic Antifungal Drugs

amphotericin B		injection, 50mg in vial
griseofulvin (8)		tablet or capsule, 125mg, 250mg
nystatin		tablet, 500 000 IU
	flucytosine(B) (1,4,8)	tablet or capsule, 250mg

8. ANTIMIGRAINE DRUGS

ergotamine (2,7)		tablet, 2mg (as tartrate)

9. ANTINEOPLASTIC AND IMMUNOSUPPRESSIVE DRUGS

azathioprine (2)		tablet, 50mg
		powder for injection, 100mg (as sodium salt) in vial
bleomycin (2)		powder for injection, 15mg (as sulfate) in vial
busulfan (2)		tablet, 2mg

Main list	*Complementary drug*	*Route of administration, pharmaceutical forms and strength*
calcium folinate (2)*		tablet, 15mg injection, 3mg ml in 10ml ampoule
chlorambucil (2)		tablet, 2mg
cyclophosphamide (2)		tablet, 25mg powder for injection, 500mg in vial
cytarabine (2)		powder for injection, 100mg in vial
doxorubicin (1,()		powder for injection, 10mg, 50mg (hydrochloride) in vial
fluorouracil (2)		injection, 50mg/ml in 5-ml ampoule
methotrexate (2)		tablet,2.5mg (as sodium salt) injection, 50mg (as sodium salt) in vial
procarbazine (2)		capsule, 50mg (as hydrochloride)
vincristine (2)		powder for injection, 1mg, 5mg (sulfate) in vial

10. ANTIPARKINSONISM DRUGS

levodopa		tablet or capsule, 250mg
trihexyphenidyl (1)		tablet, 2mg, 5mg (hydrochloride)
	levodopa+carbidopa (B) (1,5,6)	tablet, 100mg+10mg, 250mg+25mg

11. BLOOD, DRUGS AFFECTING THE

11.1 Antianaemia Drugs

ferrous salt (1)		tablet, equivalent to 60mg iron (as sulfate or fumarate)
folic acid (2)		tablet, 1mg injection, 1mg in 1ml ampoule
	iron dextran (B) (1,5)	injection, equivalent to 50mg iron/ml in 2-ml ampoule
hydroxocobalamin (1,2)		injection, 1mg in 1-ml ampoule

11.2 Anticoagulants and Antagonists

heparin (2)	injection, 1000 IU/ml, 25 000 IU/ml in 5ml ampoule
phytomenadione	injection, 10mg/ml in 5-ml ampoule
protamine sulfate (2)	injection, 10mg/ml in 5-ml ampoule
warfarin (1,2,6)	tablet, 5mg (sodium salt)

12. BLOOD PRODUCTS AND BLOOD SUBSTITUTES

12.1 Plasma Substitute

dextran 70	injectable solution, 6%

12 2 Plasma Fraction for Specific Uses

albumin, human normal (2,8)	injectable solution, 25%

**Drug for "rescue therapy" with methotrexate.*

Main List	*Complementary drugs*	*Route of administration pharmaceutical forms and strengths*
	antihaemophilic fraction (c) (2,8) (synonym: factor VIII)	(dried)
	fibrinogen (c) (2,8)	(dried)
	plasma protein (c) (2,8)	injectable solution, 5%
	factor IX complex (coagulation factors II, VII, IX, X, concentrate) (c) (2,8)	(dried)

13. CARDIOVASCULAR DRUGS

13.1 Antianginal Drugs

glyceril trinitrate		tablet (sublingual) 0 5mg
isosorbide dinitrate (1)		tablet (sublingual) 5mg
propranolol (1)		tablet, 10mg, 40mg (hydrochloride) injection, 1mg (hydrochloride) in 1ml ampoule

13.2 Antiarrhythmic Drugs

lidocaine		injection, 20mg (hydrochloride)/ml in 5ml ampoule
procainamide (1)		tablet, 500mg (hydrochloride) injection, 100mg (hydrochloride)/ml in 10-ml ampoule
propranolol (1)		tablet, 10mg, 40mg (hydrochioride) injection, 1mg (hydrochloride) in 1–ml ampoule
	quinidine (A, B) (1)	tablet, 200mg (sulfate)

13.3 Antihypertensive Drugs

hydralazine (1)		tablet, 50mg (hydrochloride)
hydrochlorothiazide (1)		tablet, 50mg
propranolol (1)		tablet, 40mg (hydrochloride)
sodium nitroprusside (1,2,8)		injection, 10mg/ml in 5ml vial
	methyldopa (A, B) (7)	tablet, 250mg
	reserpine (A) (1,7)	tablet, 0.1mg 0.25mg injection, 1mg in 1–ml ampoule

13.4 Cardiac Glycosides

digoxin (4)		tablet, 0.0625mg; 0.25 mg oral solution. 0.05mg/ml injection, 0.25mg ml in 2–ml ampoule
	digitoxin (B) (6)	tablet, 0.05mg, 0.1mg oral solution, 1mg/ml injection, 0.2mg in 1–ml ampoule

Main list	*Complementary drugs*	*Route of administration, pharmaceutical forms and strengths*
13.5 Drugs Used in Shock or Anaphylaxis		
dopamine (2)		injection, 40 mg (hydrochloride) / ml in 5-ml vial
epinephrine		injection, 1 mg (as bitartrate) in 1 - ml ampoule
	isoprenaline (c)	injection, 1mg (hydrochloride)/ml in 2–ml ampoule
14. DERMATOLOGICAL DRUGS		
14.1 Antiinfective Drugs		
neomycin+bacitracin (1)		ointment, 5mg neomycin+500 IU bacitracin zinc/g
14.2 Antiinflammatory Drugs		
betamethasone (1,3)		ointment or cream, 0.1% (as valerate)
hydrocortisone (1)		ointment or cream, 1% (acetate)
14.3 Astringents		
aluminium acetate		solution 13% for dilution
14.4 Fungicides		
benzoic acid+salicyclic acid		ointment or cream, 6%+3%
miconazole (1)		ointment or cream, 2% (nitrate)
nystatin		ointment or crsam 100 000 IU/g
14.5 Keratoplastic Agents		
coal tar		solution, topical 20%
salicylic acid		solution, topical 5%
14.6 Scabicides and Pediculicides		
benzyl benzoate		lotion, 25%
gamma benzene hexachloride		cream or lotion, 1%
15. DIAGNOSTIC AGENTS		
edrophonium (2,8)		injection, 10mg(chloride)in 1-ml ampoule
tuberculin, purified protein derivative (PPD)		injection

Main list	*Complementary drugs*	*Route of administration, pharmaceutical forms and strengths*
15.1 Ophthalmic		
fluorescein		eye drops, 1% (sodium salt)
15.2 Radiocontrast Media		
adipiodone meglumine (1)		injection, 25% in 20-ml vial
barium sulfate (1)		powder
iopanoic acid (1)		tablet, 500mg
meglumine amidotrizoate (1)		injection, 60% in 20–ml ampoule
sodium amidotrizoate (1)		injection, 50 in% 20–ml ampoule
16. DIURETICS		
amiloride (1)		tablet, 5mg (hydrochloride)
furosemide (1)		tablef, 40mg
		injection, 10mg/ml in 2–ml ampoule
hydrochlorothiazide (1)		tablet, 50mg
mannitol		injectable solution, 10%, 20%
	chlortalidone (B) (6)	tablet, 50mg
17. GASTROINTESTINAL DRUGS		
17.1 Antacids (nonsystemic)		
aluminium hydroxide		tablet, 500mg
		oral suspension, 320mg/5ml
magnesium hydroxide		oral suspension. equivalent to 550mg magnesium oxide/10ml
	calcium carbonate (A, B)	tablet, 600mg
17.2 Antiemetics		
promethazine (1)		tablet, 10mg, 25mg (hydrochloride)
		elixir or syrup, 5mg (hydrochloride)/5ml
		injection, 25mg (hydrochloride)/ml in 2-ml ampoule
17.3 Antihaemorrhoidals		
local anaesthetic, astringent and antiinflammatory drug (1)		ointment or suppository
17.4 Antispasmodics		
atropine [1]		tablet, 1mg [sulfate]
		injection, 1mg [sulfate] 1–ml ampoule

Main list	*Complementary drugs*	*Route of administration, pharmaceutical forms and strengths*
17.5 Cathartics		
senna [1]		tablet, 7.5mg [sennosides]
17.6 Diarrhoea		
17.6.1 Antidiarrhoeal		
codeine [1,10]		tablet. 30mg [phosphate]
17.6.2 Replacement Solution		
oral rehydration salts [for glucose-salt solution]		
For 1 litre of water:		[sachet] mmol/l
sodium chloride [table salt]		3.5g, Na+ 90
sodium bicarbonate [baking soda]		2.5g, HCO_3– 30
potassium chloride		1.5g, K+ 20
glucose [dextrose]		20 0g, glucose 111
18. HORMONES		
18.1 Adrenal Hormones and Synthetic Substitutes		
dexamethasone [1]		tablet, 0.5mg, 4mg injection, 4mg [sodium phosphate] in 1ml ampoule
hydrocortisone		powder for injection, 100mg [as sodium–succinate] in vial
prednisolone [1]		tablet, 5mg
	fludrocortisone [c]	tablet, 0.1mg [acetate]
18.2 Androgens		
testosterone [2]		injection, 200mg [enantate] in 1–ml ampoule injection 25mg [propionate] in 1ml ampoule
18.3 Estrogens		
ethinylestradiol[1]		tablet, 0 05mg
18 4 Insulins		
compound insulin zinc suspension [1]		iniection, 40 IU/ml in 10–ml vial, 80 IU/ml in 10–ml vial
insulin injection		injection, 40 IU/ml in 10-ml vial, 80 IU/ml in 10-ml vial

Main list	*Complementary drugs*	*Route of administration, pharmaceutical forms and strengths*

18.5 Oral Contraceptive

ethinylestradiol + levonorgestrel [1]		tablet, 0.03mg + 0.15mg, 0.05mg + 0.25mg
ethinylestradiol + norethisterone [1]		tablet, 0.05mg + 1.0mg
	norethisterone[B]	tablet, 0.35mg

18.6 Progestogens

norethisterone [1]	tablet, 5mg

18.7 Thyroid Hormones and Antagonists

levothyroxine	tablet, 0.05mg, 0.1mg [sodium salt]
potassium iodide	tablet, 60mg
propylthiouracil [1]	tablet, 50mg

18.8 Ovulation Inducer

clomifene [c] [2,8]	tablet, 50mg [citrate]

19. IMMUNOLOGICALS

19.1 Sera and Immunoglobulins

anti–D immunoglobulin [human]	injection, 0.25mg/ml
antirabies hyperimmune serum	injection, 1000 IU in 5ml ampoule
antivenom sera	injection
diphtheria antitoxin	injection, 10 000 IU, 20 000 IU in vial
immunoglobulin, human normal [2]	injection
tetanus antitoxin	injection, 50 000 IU in vial

19.2 Vaccines

19.2.1 For Universal Immunization

BCG vaccine [dried]	injection	All vaccines should comply with the WHO Requirements for Biological Substances*
diphtheria–pertussis–tetanus vaccine	injection	
diphtheria–tetanus vaccine	injection	
measles vaccine	injection	
poliomyelitis vaccine [live attenuated]	oral solution	
smallpox vaccine	multiple puncture	
tetanus vaccine	injection	

**Requirements for specific vaccines and their standards are available in various WHO Technical Reports, available on request from the WHO, Geneva.*

Main list	*Complementary drugs*	*Route of administration, pharmaceutical forms and strengths*	
		19.2.2 For Specific Groups of Individuals	
influenza vaccine		injection	All vaccines should comply with the WHO Requirements for Biological Substances*
meningococcal vaccine		injection	
rabies vaccine		injection	
typhoid vaccine		injection	
yellow fever vaccine		injection	

20. MUSCLE RELAXANTS (PERIPHERALLY ACTING) AND CHOLINESTERASE INHIBITORS

neostigmine (1)		tablet, 15mg (bromide) injection, 0.5mg (metilsulfate) in 1–ml ampoule
suxamethonium (2)		injection, 50mg (chloride)/ml in 2–ml ampoule
tubocurarine (1,2)		injection, 10mg (chloride) ml in 1.5ml ampoule
	pyridostigmine (B) (2,8)	tablet, 60mg (bromide) injection, 1mg (bromide) in 1-ml ampoule

21. OPHTHALMOLOGICAL PREPARATIONS

21.1 Antiinfective

silver nitrate		solution (eye drops) 1%
sulfacetamide		eye ointment, 10% (sodium salt) solution (eye drops), 10% (sodium salt) eye ointment, 1% (hydrochloride)

21.2 Antiinflammatory

hydrocortisone (2,7)		eye ointment, 1% (acetate)

21.3 Local Anaesthetics

tetracaine (1)		solution (eye drops), 0.5% (hydrochloride)

21.4 Miotics

pilocarpine		solution (eye drops), 2%, 4% (hydrochloride or nitrate)

21.5 Mydriatics

homatropine (1)		solution (eye drops), 2% (hydrobromide)
	epinephrine (A,B) (2)	solution (eye drops), 2% (as hydrochloride)

*Requirements for specific vaccines and their standards are available in various WHO Technical Reports, available on request from the WHO, Geneva.

Main list	*Complementary drug*	*Route of administration, pharmaceutical forms and strength*
	21.6 Systemic	
acetazolamide		tablet, 250mg
	22 OXYTOCICS	
ergometrine (1)		tablet, 0.2mg (maleate) injection, 0.2mg (maleate) in 1-ml ampoule
oxytocin		injection, 10 IU in-ml ampoule
	23. PERITONEAL DIALYSIS SOLUTION	
intraperitoneal dialysis solution (of appropriate composition)		parenteral solution
	24. PSYCHOTHERAPEUTIC DRUGS	
amitriptyline (1)		tablet, 25mg (hydrochloride)
chlorpromazine (1)		tablet, 100mg (hydrochloride) syrup, 25mg (hydrochloride) / 5ml injection, 25mg (hydrochloride)/ml in 2-ml ampoule
diazepam (1)		tablet, 5mg
fluphenazine (1,5)		injection, 25mg (decanoate or enantate) in 1-ml ampoule
haloperidol (1)		tablet, 2mg injection, 5mg in 1-ml ampoule
lithium carbonate (2,4,7)		capsule or tablet, 300mg
	25.1 RESPIRATORY TRACT, DRUGS ACTING ON THE	
	25.1 Antiasthmatic Drugs	
aminophyline (1)		tablet, 200mg injection, 25mg/ml in 10–ml ampoule
epinephrine		injection, 1mg (as hydrochloride) in 1–ml ampoule
salbutamol (1)		tablet, 4mg (sulfate) oral inhalation (aerosol), 0,1mg (sulfate) per dose syrup, 2mg (sulfate)/5ml

Main List	*Complementary drugs*	*Route of administration pharmaceutical forms and strengths*
	beclometasone (B) (8)	oral inhalation (aerosol), 0.05mg (dipropionate) per dose
	cromoglicic acid (B) (2, 8)	oral inhalation (cartridge), 20mg (sodium salt) per dose
	ephedrine (A)	tablet, 30mg (as hydrochloride) elixir, 15mg (as hydrochloride)/5ml injection, 50mg (sulfate) in 1-ml ampoule
	25.2 Antitussives	
	codeine (10)	tablet, 10mg (phosphate)

26. SOLUTIONS CORRECTING WATER, ELECTROLYTE AND ACID-BASE DISTURBANCES

26.1 Oral

oral rehydration salts (for glucose-salt solution)	For composition, see 17.6.2 *Replacement solution*
potassium chloride	oral solution

26.2 Paranteral

compound solution of sodium lactate	injectable solution
glucose	injectable solution, 5% isotonic, 50% hypertonic
glucose with sodium chloride	injectable solution, 4% glucose, 0.18% sodium chloride (Na+30 mmol, Cl–30 mmol l)
potassium chloride	injectable solution
sodium bicarbonate	injectable solution, 1.4% isotonic (Na+ 167 mmol/l, HCO_3 – 167 mmol/l)
sodium chloride	injectable solution, 0 9% isotonic (Na+ 154 mmol/l, Cl–154 mmol/l)
water for injection	in 2-ml, 5-ml, 10-ml ampoules

27. SURGICAL DISINFECTANTS

chlorhexidine (1)	solution, 5% (gluconate) for dilution
iodine (1)	solution, 2.5%

28. VITAMINS AND MINERALS

ascorbic acid	tablet, 50 mg
ergocalciferol (1)	capsule or tablet, 1.25 mg (50 000 IU)

Main list	*Complementary drugs*	*Route of administration, pharmaceutical forms and strengths*
		oral solution, 0 25 mg/ml (10 000 IU)
nicotinamide (1)		tablet, 50 mg
pyridoxine		tablet, 25 mg (hydrochloride)
retinol		capsule or tablet, 7 5 mg (25 000 IU), 60 mg (200 000 IU)*
		oral solution, 15 mg/ml (50 000 IU)
riboflavin		tablet, 5 mg
sodium fluoride		tablet, 1.1 mg
thiamine		tablet, 50 mg (hydrochloride)
	calcium gluconate (c) (2, 8)	injection, 100 mg/ml in 10-ml ampoule

SUGGESTED BASIS FOR SELECTION OF DRUGS TO CONSTITUTE COMMUNITY HEALTH CARE CENTRE FORMULARY

acetysalicylic acid	benzoic acid+salicylic acid skin ointment
paracetamol	benzyl benzoate
metronidazole	aluminium hydroxide
mebendazole	promethazine
piperazine	senna
ampicillin	oral rehydration salts (for glucuose-salt solution)
sulfadimidine	BCG vaccine
tetracycline	diptheria-pertussis-tetanus vaccine
diethylcarbamazine	measles vaccine
chloroquine	poliomyelitis vaccine (live attenuated)
pyrimethamine	tetanus vaccine
isoniazid	silver nitrate eye drops
streptomycin	sulfacetamide eye ointment
ferrous salt	ergometrine
folic acid	iodine
hydroxocobalamin	ascorbic acid
neomycin+bacitracin skin ointment	ergocalciferol

**For use in the treatment of xerophthalmia with a single dose, not to be repeated before 4 months have elapsed.*

Courtesy :- 'CONTACT', the bimonthy bulletin & the Christians medical commission & the World council of churches, Geneva